A Physician's Manual of Vaccine Therapy

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ROBERT L. PHILLIPS, M.D.

A PHYSICIAN'S MANUAL *of* VACCINE THERAPY

By
G. H. SHERMAN, M. D.

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G. H. SHERMAN, M. D.
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Preface

THIS little book purports to give in a concise, comprehensive manner such facts and data as are pertinent to the application of Bacterial Vaccine Therapy in the prophylaxis and treatment of infectious disease.

In order to make the data conveniently available for reference, it has been arranged alphabetically and titled according to disease.

The facts and data given are the result of seventeen years of study and specialized effort in addition to a great deal of research work and also clinical investigation carried on in hospitals, sanitoria, etc.

Great credit is due the men who have cooperated in this work and who, in a large measure, made this authentic information possible.

As the title indicates, it is a manual and most necessarily then should be concise, convenient and practical. The section on Bacteriology does not intend to give complete information on the subject, but it does give that information which the practitioner may require at the moment in the application

of this important therapy. There are many complete works on Bacteriology which can be consulted for more complete information on the subject.

Necessarily in a manual of this nature considerable repetition is unavoidable and advisable to provide at the point of reference the general information sought for on the point in question; otherwise considerable back reference would be necessary and would in a measure defeat the purpose of the book.

The Appendix proposes to present from the literature such material chosen at random as may be of general interest to the reader using this form of therapy as an adjunct in his practice. Much more could be added but it would hardly add materially to the usefulness of the book when considered as a manual.

In brief, if this book provides concise, comprehensive and practical data on the application of Bacterial Vaccine Therapy in the prophylaxis and treatment of infectious disease, it will serve its purpose.

There is a Difference in Vaccines

DURING the past seventeen years in addition to our own research and investigations on the subject of bacterial vaccine therapy and allied subjects we have made a most careful study of the literature on vaccine therapy. We have not only studied the reports which dealt favorably with the subject, but have made it a particular point to read and study the reports in which vaccine therapy was criticized. Coming in contact with thousands of physicians, we have of necessity heard not only favorable comment but also almost every conceivable objection. Consequently we believe we can speak authoritatively on the subject of vaccine therapy.

Our observations have convinced us that many of the criticisms adverse to bacterial vaccines have in a large measure been justified. There are certain cardinal conditions necessary to obtain results with vaccines and unless all the conditions are fulfilled, nothing but mediocre success or failure is possible.

Many of the vaccines which were used were lacking in antigenic qualities; they were not standardized so that uniform results whether good or bad could be obtained. Formulæ were selected without regard to the actual bacterial flora in the infection to be combated. The value of collateral or nonspecific immunity was ignored in the single organism vaccines and the specificity of the immunizing mechanism was ignored by those who could only see the non-specific reaction with the result that they used vaccines entirely unrelated to the actual infecting organisms.

The dosage used and interval of inoculation were based on theoretical consideration rather than on ascertained clinical fact.

The fear of adding more toxic material to a patient already overtaxed with toxic substance was the stumbling block to a rational dosage. It became almost an axiom that the more acute the infection the smaller the dose and the longer the interval. Experience has shown that the proper procedure is to give larger doses at shorter intervals in acute toxic infections.

Under the circumstances many unfavorable reports on the use of vaccines emanated from men who used formulæ and dosage with which no experienced vaccine therapeutist would expect to obtain results. Why so many good men should try methods which have repeatedly ended in failure and not at least investigate the methods used by those who are obtaining results is beyond comprehension.

One more word as to the reason for the failures in vaccine therapy: The question of efficient vaccines.

Bacteria are particularly susceptible to the type of culture media on which they grow. If grown on plain agar or bouillon the streptococcus, pneumococcus and some other organisms lose their virulence quite rapidly. In addition to losing their virulence they undoubtedly also lose some of their bio-chemical characteristics. There has been much said about the individual variations in the different strains of streptococci. We are of the opinion that the variation in the bio-chemical construction of the streptococcus hemolyticus and viridans is less than the variation in bio-chemical construction of either organism when growing in the human body and the ordinary culture media used for growing vaccines. In other words stock vaccines made from old cultures grown on simple culture media are different in their protein construction from organisms growing in the human body and cannot be expected to excite an identical immunizing response.

Work done at the Pasteur Institute and elsewhere has shown that when a culture is grown on media enriched with the blood serum or tissue of an animal the culture becomes virulent for that animal.

Following the careful selection of cultures for the preparation of Sherman's Stock Vaccines, the cultures are carried in media enriched with human blood serum. All our stock suspensions are grown on this enriched media so the organisms therein should be more nearly identical with the organisms in human infection and should produce a more specific and adequate immunizing response. The low toxicity and high antigenic properties of Sherman's Vaccines which distinguish them from others is undoubtedly due in part to our method of cultivating them.

Heat is generally conceded to be deleterious to biological products. If heat is deleterious to vaccines, why are all other stock bacterial vaccines sterilized with heat? If ordinary room temperatures are deleterious what will 55°, 65° or maybe even occasionally 70° centigrade do to the potency of a vaccine?

Numerous workers, among whom might be mentioned Dr. Kolmer, are of the opinion that heat is deleterious to bacterial vaccines.

Sherman's Bacterial Vaccines have been sterilized without heat for many years.

The question of standardization and methods of standardization is also of importance. The most common methods are Wright's comparison with blood cells, the counting chamber, opacity comparison with standard suspensions and the centrifuge method with Hopkins' vaccine tube.

Each method undoubtedly has certain advantages from the standpoint of time, accuracy, etc.

Wright's method and the counting chamber are both slow. Opacity comparison whether done against standard suspensions of bacteria or barium suspensions are extremely subject to the personal equation. Light conditions, eyesight, personal judgment, all influence the final result. It would be very difficult to get several different groups of workers with the opacity method to produce vaccines of uniform strength. Examinations of vaccines standardized in this manner have shown them to be both greatly undercount and overcount.

The Hopkins method may serve a purpose but is open to the criticism that if the organisms are grown in fluid media the fine precipitates that form will be thrown down with the bacteria and counted as bacterial substance. The same might occur with small particles of agar.

The number of organisms per cubic centimeter in a 1 percent suspension as given by Hopkins in the Journal A. M. A., 1913, IX, 1615 which has been quoted extensively is as follows:

Streptococcus hemolyticus—8 billions per cubic centimeter.
Staphylococcus aureus and albus—10 billions per cubic centimeter.
Gonococcus—8 billions per cubic centimeter.
Pneumococcus—2.5 billions per cubic centimeter.
B. Typhosus—8 billions per cubic centimeter.
B. Coli—4 billions per cubic centimeter.

Most text books give the size of the streptococcus as 0.4 to 1 micron and the typhoid bacillus as 1 to 3 microns long and 0.5 to 0.8 micron in diameter. How these two organisms which are so widely different in size can occupy the same space in the Hopkins tube is hard for us to understand.

It is also hard for us to believe that the pneumococcus is on the average four times as large as the staphylococcus.

B. Coli according to the Hopkins tube is twice the size of the typhoid bacillus.

As the Hopkins and opacity methods are extensively used in the standardizing of vaccine suspensions how are we going to decide or compare from a dosage standpoint the results obtained by different observers in the use of vaccines? Some workers have reported severe reactions from the subcutaneous injection of doses of 5 million organisms. In view of what we have observed of such standardizing of vaccines, particularly autogenous, we would hazard a guess that the strength of the vaccine was guessed at and probably contained several billions of bacteria instead of a few million.

We have made it a uniform practice to count all our vaccine suspensions by Wright's method, three individual counts being made by different laboratory workers. These counts must approximate and then the average of the three counts is taken as the count.

The older text books on bacteriology did not make any particular differentiation between the Influenza Bacillus and Bacillus Pertussis. It was thought that the organisms were almost identical. (Park & Williams 1910 Ed. P. 484.)

Laboratory workers when in need of Influenza B. cultures had recourse to whooping-cough cases. After the influenza epidemic of 1918 we collected quite a number of cultures which were used in the production of vaccine during the epidemic We were surprised to find that a number of these cultures grew well on media which did not contain hemoglobin. As near as we could classify them they were not B. Influenza at all but whooping-cough bacilli. As these cultures grow more readily than the influenza bacillus they undoubtedly were the predominant organism in many so-called influenza vaccines. Of course any investigation conducted with vaccines of this nature to determine the value of influenza vaccine would prove nothing but that that vaccine was valueless.

From these observations we might say that the criticism against mixed vaccines has been due to faulty concepts as to selection of vaccine, improper dosage, and the use of products unscientifically prepared and lacking in antigenic properties.

Our efforts have been directed particularly to the development of bacterial vaccines which would be efficacious against infections caused by the streptococcus, pneumococcus, staphylococcus, colon bacillus, micrococcus of catarrh, bacillus influenza and the Friedlander Bacillus or groups of these organisms in mixed infections, because these organisms cause such a large proportion of all disease and death.

The streptococcus, for instance, can cause a primary infection in practically any part of the human body. Erysipelas, mastoiditis, appendicitis, nephritis, pneumonia, lymphangitis and cellulitis are generally conceded to be due to the streptococcus. Rheumatism frequently is caused or aggravated by this organism. It is a most common secondary invader complicating the treatment of many diseases. The pneumococcus, while not as diversified in its activities is nevertheless a very serious and dangerous infecting organism. A large percentage of the pneumonias are probably directly caused by it. In conjunction with the streptococcus, this organism is responsible for approximately 100,000 deaths annually from pneumonia alone.

The staphylococcus, while not causing as many fatal diseases as these other organisms, is still responsible for many secondary infections, which undoubtedly aid the streptococcus and pneumococcus in maintaining themselves in the tissues of the body. The same is true of the micrococcus of catarrh, colon and the Influenza bacilli, as these organisms grow in symbiosis with the more virulent ones.

Fully two-thirds of the infections which the medical profession is called on to treat are due to or complicated by one or more of these organisms.

Many hundreds of physicians have demonstrated to their entire satisfaction that it is possible to produce immune substances in appreciable amounts for therapeutic purposes against these organisms during an infection within 24 hours after an inoculation of an appropriate vaccine. It was formerly believed that immune bodies were not produced until a considerable period of time had elapsed. Recent work by Wright has conclusively shown that immune bodies are produced in appreciable quantities within a few hours after the vaccine inoculation. This has been demonstrated clinically in pneumonia where it is possible by giving the vaccine on the first day of the disease to produce a normal temperature in a large proportion of the cases in 48 hours.

This can be done with sufficient uniformity to entirely do away with any possibility of coincidence being responsible for the results. Even in cases of pneumonia in which the vaccine treatment is started late in the course of the disease when the patient is thoroughly overwhelmed with toxic substances and theoretically, the tissues have already responded to their maximum immuno production, it is still possible to obtain a decided degree of therapeutic response.

At several hospitals a series of pneumonia cases were treated under control conditions giving an average mortality rate of the controls as 38.0% and the vaccine treated cases as 23.3%. These were practically all severe advanced cases before vaccine treatment was started.

It is interesting to note in this connection that at these hospitals, our mixed vaccine formula 38 was administered in 1 to 2 c.c. doses at 6 to 12 hour intervals, depending upon the severity of the case, the largest dose being used in those cases which showed the most profound toxemia and depression.

The vaccine treatment of pneumonia is practically parallel to the treatment of diphtheria with antitoxin. The most marked results are obtained in the early stages of the disease.

The epidemic of pneumonia which occurred in the Army camps prior to the influenza epidemic was very severe and showed a high mortality, particularly among the troops who had measles.

Dr. Arthur Dare at Fort Oglethorpe encampment, by using the mixed vaccine early in the course of the disease was able to reduce the mortality of these pneumonias to 6.3%.

Dr. D. H. Montgomery, of Denver, Acting Assistant Surgeon, U. S. Public Health Service, in the Alaska Influenza Epidemic Expedition, makes a Biologic Report on 958 cases, selected from over 3,000 cases of

influenza and pneumonia attended in the epidemics of 1918, 1919 and 1920 (The Bacterial Therapist, March 1923) which conclusively shows by comparison of results obtained, the superior qualities of Sherman's non-heat killed bacterial vaccines over other preparations that he employed.

Under Resume he says:

"A good chemically killed vaccine used at the onset of influenza and pneumonia with temperatures as high 103.5°, will abort the disease and on the following day there will be a normal temperature in over 75% of the cases.

"85% of these cases were normal on the day following the second dose in which the temperatures at the first visit were 103° to 104.5°. In this group of cases I find that nearly all are unmistakably diagnosed influenza pneumonia.

"More than 97% of the cases are normal after the third inoculation.

"Bacterial vaccines sterilized with heat have a lower potency, will disintegrate and lose their physiological activity and become cloudy when carried in the bag for a short time.

"Vaccines sterilized without heat are much more potent and physiologically active, do not have to be kept on ice and are active therapeutically after being carried around for six months or more."

We confidently believe that it will be possible to reduce the average mortality of pneumonia throughout the country to less than 5% by the timely and adequate use of bacterial vaccines. This, in itself, is a worthy contribution to contemporary medicine, but when it is realized that these pneumonias are due to the same group of organisms that are responsible for most of the other infections of the respiratory tract, sinus infections, eye infections, ear infections and that the same immunizing mechanism can be activated to overcome infections by these organisms, no matter where the location of the infection may be, it is at once apparent that vaccine therapy opens untold fields for the rapid cure of infective processes and the alleviation of untold human misery.

In trying to appraise the value of these remedial agents, we have always tried to be conservative and not be carried away by undue enthusiasm.

By coming in contact with thousands of physicians and discussing this subject from many angles the first flush of enthusiasm has long since worn off. The novelty of a new idea burns less brightly after seventeen years unless there is exceptional merit to the idea.

We believe that we have arrived at an accurate appraisal of what can actually be accomplished with bacterial vaccines.

It is interesting to note that the Sherman Laboratory has stood almost alone in this country in the advocacy of mixed vaccines in the treatment

of acute infections. That we have never deviated from the fundamental position taken in the early days of vaccine therapy and that our contentions have been substantiated. That we have not tried to produce any trade-marked or proprietory variations of a standard product. That most of the favorable literature on the use of mixed stock vaccines has come from those physicians who have used our vaccines and followed our recommendations. That there is not a single report in the literature of anyone using our vaccines as we recommend that they should be used who has not favorably reported on the same and this in spite of the fact that many millions of doses of our vaccine have been administered.

IMMUNIZATION

IT IS now well known that most diseases are caused by infecting organisms which cripple or disturb the natural functions of the various organs of the body. Resistance to infection by pathogenic bacteria is what constitutes immunity. Immunity may be natural or acquired. Natural immunity constitutes a condition in which a certain specie will not become infected by pathogenic bacteria which will infect some other specie. Animals, for example, are naturally immune to typhoid bacillus infection while man is not. Acquired immunity constitutes a condition in which a susceptible person or animal becomes immune while overcoming an infection or by vaccination. With some pathogenic bacteria an acquired immunity usually lasts through life like in smallpox, measles, scarlet fever, chicken pox, whooping cough and mumps. With other infecting bacteria the immunity which develops while overcoming the infection will wear off in the course of a few months or a few years, after which the same susceptibility to the same bacteria will again prevail. In some instances enough immunity develops to overcome the infection but after this immunity wears off the person often becomes more susceptible to the same infecting organism. This is particularly noticeable in cases of erysipelas and pneumonia. To some pathogenic bacteria immunity is slowly and sparingly developed as is the case with the gonococcus. Frequently sort of a balance between the activities of the infecting organism and the tissues is established when the infection becomes chronic. If the infecting organism is very active, with destructive properties and multiplies rapidly, life may be destroyed within a few days by virtue of the extreme bacterial intoxication which develops. On the other hand, life may be destroyed from the suspension of the function of some important organ as the result of the organ becoming infected, as, for example, in cases of acute nephritis.

Much work has been done to determine the nature of a bacterial intoxication. From experimental data and from close observations of

clinical infections it has been found that the ferment producing concept more closely fits into what actually takes place during the course of an infection than any of the other theories that have been advanced. This ferment intoxication concept is based on the fundamental fact that germs must produce or secrete ferments to prepare or digest the food on which they live and that this digestive capacity really furnishes the only means of defense which the germ possesses and constitutes the main element of the destructive process which develops during an infection. As a whole, in the main, virulence of an organism depends on rate of multiplication, and rate of multiplication depends on the effectiveness of the ferment which the germ secretes to prepare or digest the food on which it lives. This ferment is secreted from the surface of the germs so the germs really surround themselves with this ferment and the digestion then becomes a contact process. The germs literally digest their way into the tissues they invade.

All tissues of the body are endowed with the power of developing a resistance to germ invasion when such germ invasion is not sufficiently destructive to cripple the defensive capacity of the tissues which are involved. This is accomplished by the formation of protective ferments or antibodies which have a destructive influence on the infecting organisms as a result of the infection. When this has been accomplished an active immunity has become established.

The tissues of the body are so constituted that a foreign protein (germs are composed of protein) substance is not tolerated and to dispose of it, ferments are produced which digest or destroy this foreign protein. Any substance which will cause the production of ferments which will destroy the substance itself when introduced into tissues or fluids of the body is an antigen. So it will be seen that the contest which develops during the progress of an infection is really a contest between the ferments which the germs produce to digest the food on which they live and the protective ferments which the living tissue cells produce to destroy the germs which are responsible for the infection.

A number of these protective ferments have been identified by the manner in which they influence germ destruction. When a protective ferment causes germs to form clumps, it is called an agglutinin; when it causes a precipitate, it is called a precipitin; when it dissolves germs, it is called a lysin; when it so influences germs that they become particularly susceptible to phagocytic destruction, it is called an opsonin. There are no doubt still other methods of action by these tissue-produced, protective ferments which have not as yet been ascertained. There is every reason to believe that the main action of these protective ferments consists in neutralizing the ferment with which the germ surrounds

itself and employs to digest the food on which it lives and thereby robbing it of its only means of defense by putting its digestive apparatus out of commission.

This antibody producing capacity or antigenic influence of an infecting organism is in direct proportion to its virulence to the particular person infected, the greater the virulence the less this antigenic influence, the degree or intensity of the immunity established being just as great from overcoming the less virulent germs as from a recovery from a very severe infection. This knowledge, that the less virulent organisms confer as great an immunity as the more virulent types, led to the practice of prophylactic inoculations which is so successfully employed in the prevention of smallpox. Pasteur accidentally discovered that chicken cholera germs that had been cultivated under unfavorable conditions, no longer produced ill effects when inoculated into healthy chickens, but at the same time immunized the chickens against the virulent chicken cholera organisms. This discovery laid the foundation for prophylactic immunization with attenuated organisms. It was somewhat later discovered that this attenuating process is not necessary but that it is better to kill the virulent organisms either by heat or preferably by means of dilute solutions of trikresol or carbolic acid and it was this discovery that really placed vaccine therapy on a practical basis for treating the ailments to which man is subjected.

The first question that presents itself is, how can killed germs immunize when injected under the skin? This whole problem of immunity is a problem of cell training to produce protective ferments of a particular kind which will destroy germs of the same kind that are instrumental in influencing these cells to produce these protective ferments. Germs that are very virulent to the infected individual are not suited as agents for favorably influencing the cells of that individual for protective ferment or antibody formation because the influence of virulent germs is too destructive to the cells with which they come in contact. The athlete does not develop strength by attempting the most difficult tasks first. That would cause fatigue with disastrous results. By doing the lesser tasks first strength is developed to make the more difficult tasks possible. The same rule applies to developing cell resistance to infecting bacteria. If tissue cells are invaded by very virulent germs, germs that are capable of secreting a very effective ferment which they employ to digest the food on which they live, the cells with which these germs come in contact stand a rare chance of surviving. The task is too severe for them. But if these tissue cells are brought in contact with less virulent or killed germs their defensive faculty is aroused, and since the task is not too great, the power of resistance is increased by developing the faculty of producing protective ferments or antibodies to destroy these germs and

meantime they develop the faculty of being able to attack and destroy virulent germs of the same kind. In case killed germs, in the form of a bacterial vaccine, are injected under the skin, the tissues into which the bacterial vaccine is injected set up a protest against this intrusion and tissue cell activities become aroused to get rid of these injected killed germs. These injected killed germs possess the same biochemical construction as live germs of the same kind but being killed are deprived of the power of secreting destructive digestive ferments and multiplying in number. The tissue cells, however, act upon them just the same as if an active infection by these same germs had been started. This is accomplished by the production of a ferment by these tissue cells which will digest or aid the leukocytes in digesting these germs. When tissue cells are once aroused in their capacity for producing ferments or antibodies in the process of getting rid of intruding germs whether they have been injected with a hypodermic needle or have gained entrance otherwise, they continue to do so for some considerable time thereafter and thus establish an immunity. By repeating the injection of a suitable number of killed germs at proper intervals as taught by experience this immunity can be built up to a degree of efficient intensity. This is the method which is now being so successfully employed in the prevention of typhoid fever, whooping cough, colds, cholera, bubonic plague, and many other diseases.

Therapeutic Immunization

This question of prophylactic immunization by injecting killed germs is readily understood, but when we come to the problem of immunization after an active infection has already taken place to aid them in overcoming the infection, further consideration becomes necessary. In the first place, it is necessary to realize that infections do not involve the entire body. As a rule the infection is confined to a definite part of the body or some special organ like the lung, kidney, liver, appendix, tonsil, skin, joints, mucus membranes, etc. Even in the so-called general infections where the circulating blood is infected, the great mass of body tissues remain uninvolved except where the infection happens to localize. So we see that in case of an infection, a major portion of the body is not actively attacked by the invading bacteria. During the immunizing process the infected portion of the body is mainly relied upon to produce the protective ferments or antibodies to get rid of the infection. That is, the infected tissues must come to their own rescue in overcoming the infecting bacteria. This is not always possible. If the infecting bacteria are sufficiently active with their ferment production to cripple the defensive faculty of the involved tissues, immunization will be retarded or suspended with a resulting prolonged illness or a fatal termination.

If then, bacterial vaccines are injected under the skin remote from the infected area composed of killed organisms like those responsible for the infection, protective ferments (antibodies) are produced by the tissue cells into which the killed bacteria are injected. These protective ferments are then conveyed by means of the circulating medium to the infected area and there aid the involved tissues in overcoming the infection. In other words, healthy tissues are induced and made use of to produce protective ferments to aid the infected tissues in their battle with the destructive bacteria.

That this actually takes place is readily demonstrated clinically, especially so when bacterial vaccines are given during the early stages of an acute infection. Let us take as an illustration a case of lobar pneumonia during its early stages. Here we have a condition in which the pneumococcus is found in the blood and the infection localizing in the lung tissues about the time of the initial chill with pain in the chest, followed by high fever, rapid pulse, and coughing up blood-streaked mucus. Every practitioner of clinical experience knows that such a combination of symptoms means the beginning of a lobar pneumonia. If a combined bacterial vaccine containing the various types of pneumococci and streptococci is given within three or four hours in suitably large dosage and repeated at 12 to 24-hour intervals for several days or more, the infection will in a large majority of cases be aborted and the case go on to recovery within 3 to 5 days. Similar results are obtained in cases of acute lymphangitis, tonsillitis, rhinitis, otitis media, mastoiditis, etc. Such clinical results are evidently due to rapid protective ferment (antibody) production as a result of the bacterial vaccine injection. That the lymphatic internal organs, as some contend, are responsible for this protective ferment formation is not established. From this contention it must be assumed that it is the general bacterial intoxication which follows an infection which influences the internal lymphatic organs for this protective ferment production. It may be true that in severe cases of infection the internal lymphatic organs eventually come to the rescue, but at best this is a slow process which only too often results in a fatal termination. This concept would imply that the toxic material contained in a dose of bacterial vaccine would add sufficient bacterial intoxication to induce the internal lymphatic organs to produce protective ferments (antibodies). This cannot be possible because as a rule we have excessive bacterial intoxication and this bacterial intoxication often progressively increases until death ensues. Furthermore, bacterial vaccines are given in such infinitesimal dosage that when injected under the skin no appreciable toxic reaction as shown by temperature or pulse rate is produced. About .0004 of a grain of killed germs is an average dose. This is evidently a minute fraction as compared to the bacterial poisons already

present and being produced every hour as the infection progresses and, consequently, could not be instrumental in influencing the internal lymphatic organs in any way. But at the site of bacterial vaccine injection the killed bacteria are deposited in the subcutaneous tissues in a rather concentrated form and there cause a local irritation as shown by the inflammatory reaction at that place. Evidently these subcutaneous tissues are being influenced in their defensive capacity. The injected killed germs bear a relation to these tissues similar to a localized infection by the same kind of germs as those contained in the vaccine, the only difference being that these killed germs are deprived of the power of multiplying and secreting toxic destructive ferments. By properly gauging the dose this local tissue reaction may be developed to a point where the greatest amount of defensive activity is aroused; a point where the tissue cells are not fatigued by excessive bacterial intoxication and yet enough to bring forth a maximum amount of protective ferment (antibody) formation by these tissues. In other words, by this means tissue cells may be stimulated to their utmost capacity for the formation of protective ferments. These protective ferments are then absorbed by the circulating medium and thus conveyed to the infected area, where the involved tissues are aided in destroying the infecting bacteria.

It is found that the very best results from bacterial vaccine injections are obtained during the very early stages of an infection. Bacteria like all other living things are endowed with this universal law of developing resistance to survive and thereby become immune to substances that otherwise would be destructive to them. During the early stages of an infection every advantage presents itself for therapeutic immunization. First, the infecting bacteria have not had time to immunize themselves to the protective ferments (antibodies) of the infected individual. Second, they are less in number and consequently it requires less protective ferment (antibodies) to destroy them. Third, tissue cells are less capable of being induced to protective ferment (antibody) production after they have been fatigued by excessive bacterial intoxication and, fourth, the infection has not had time to cause as much destruction at the site of infection and consequently less repair is necessary to restore normal functions. When bacterial vaccines are given during the early stages of an infection distinct evidences of immuno development are seen within 18 to 36 hours by a reduction in temperature, improved pulse rate and a noticeable improvement in the infected area. No such rapid improvements are observed in severe far-advanced infections although decided improvement is often observed soon after giving the vaccine and not infrequently, apparently hopeless cases eventually recover. For this reason no case should be abandoned but therapeutic immunization should

be instituted even in the worst kind of cases. The treatment is absolutely harmless even in severe advanced cases.

A chronic infection is a condition where the resistance of the infecting bacteria to the protective substances of the body has developed to a point where the germ may maintain itself and continue to prolong the infection indefinitely. In these chronic infections a central focus of low resistance often develops which will develop sufficient resistance to eradicate the infecting bacteria very tardily and if accessable such foci should be treated surgically, therapeutic immunization being at the same time instituted to hasten recovery. Where the infection is such that surgery is not applicable, therapeutic immunization with bacterial vaccines may be relied upon as the best means to eradicate the infection. This is best illustrated in cases of chronic bronchitis, arthritis, neuritis, cystitis, gastritis, sinusitis, etc. Treatment must be started with small doses because these chronic cases are usually rather sensitive to bacterial vaccine injections, reactions with considerable inflammation at the site of injection being common. The dose should be so gauged that a red spot about the size of a silver dollar develops at the site of injection. The initial dose is usually about 0.2 c.c. of Sherman's standard suspensions. The dose is then increased by 0.1 or 0.2 c.c. each subsequent treatment until the dose is worked up to 1.0 c.c. As a rule the inflammatory reaction at the site of vaccine injection will become less as the dosage is increased. If this reaction should become worse under increasing dosage, it would indicate that the doses are too large and smaller doses should be employed. Injections should not be repeated in chronic infections until the inflammation from the previous injection has well subsided. This will take anywhere from 3 to 7 days. In most chronic conditions inoculations are best made at 5 to 7 day intervals. Most of these cases will not tolerate crowding. It is much better to gauge the doses so no marked reaction develops and persistently continue the treatment often for 6 months, a year or more.

A MULTIPLICITY OF DISEASES PRODUCED BY A FEW VARIETIES OF GERMS

WHEN considering bacterial infections, we must keep in mind that we have a large variety of diseases caused by a comparatively few varieties of disease-producing germs. Health is maintained by a proper co-ordination of the functions of the various parts and organs of the body. If the function of any one organ is interfered with, symptoms will develop that do not conform to the normal standard. If the function of the liver is disturbed, we have symptoms that are entirely different from a disturbance of the function of the kidneys. So we

may have a gastritis, cystitis, appendicitis, neuritis, arthritis, iritis, otitis, sinusitis, bronchitis, endocarditis, peritonitis, meningitis, rhinitis, pharyngitis, tonsillitis, conjunctivitis, dermatitis, lymphangitis, producing different symptoms in each diseased condition but all being produced by a streptococcus. In reality, the streptococcus is capable of infecting almost any part of the body and thereby cause a corresponding disease. What is true of the streptococcus in this respect, in a large measure also holds good with the pneumococcus and staphylococcus. Mixed infections by these various organisms are exceedingly common in most of these infections. From this it is clear that the bulk of the disease conditions met with in everyday practice, and by adding the colon bacillus to the list which is a common infective agent either as a primary invader or a complicating factor in infections of the abdominal viscera and pelvic organs, we cover a large majority of the diseases met with in the general routine of practice and from an immunologic standpoint must be treated as infections by these various organisms regardless of the part of the body or organ that is involved. While the streptococcus, pneumococcus and staphylococcus are liable to infect any part of the body yet there are certain parts of the body in which the infections by these organisms are more prevalent. In infections of the tonsils, pharynx and middle ear, streptococci prevail. In the nasal mucus membrane and lung the pneumococci are most prevalent. Skin infections are most commonly due to staphylococci. In infections of the gall bladder, pelvis, the kidney and bladder, the colon bacillus usually predominates. In the respiratory tract we also find the micrococcus catarrhalis, Friedlander bacillus and the influenza bacillus as common invaders when either or all of these germs are present they are usually in association with pneumococci, streptococci and staphylococci. So in reality the latter three organisms are the real serious offenders. The same condition prevails in infections of the pelvic organs and abdominal viscera where colon bacillus infections prevail, staphylococci, streptococci and pneumococci are also liable to be present. So, when instituting therapeutic immunization, it is always well to bear in mind the prevailing infecting bacteria in the portion of the body involved. In infections of the respiratory tract we have the streptococcus, pneumococcus, and staphylococcus with the micrococcus catarrhalis, influenza bacillus or Friedlander bacillus added. In the abdominal cavity and pelvis, the three prior organisms with the colon bacillus added and in skin infections primarily the staphylococcus aureus and albus.

In addition to the main general infections enumerated above, we have special infections which are very common. Of these, tubercle bacillus and gonococcus infections are the most common and serious. But when considering even these infections, we find that as a rule these

infections assume serious proportions after staphylococci, streptococci, or pneumococci become complicating factors of the infection. In gonorrhea, staphylococci make their appearance early in the discharge and in the chronic cases staphylococci, streptococci, pneumococci and colon bacilli become the dominant factors of the infection. In bone tuberculosis staphylococci make their appearance and are a prominent factor of the destructive process. Mixed infections are a predominating factor in pulmonary tuberculosis in which the prevailing infecting bacteria of respiratory infections are real pathogenic factors. It is an open question whether the tubercle bacilli or the mixed infections in pulmonary tuberculosis do the greater amount of harm. To institute therapeutic immunization in cases of tubercle infection without taking into account the mixed infections is certainly not logical and from clinical experience not justified.

Whooping-cough is a special infection due to the Bordet bacillus. Whooping-cough is now being successfully prevented and cured by vaccine injections. The greatest source of danger in whooping-cough is broncho-pneumonia. In this connection it is necessary to know that this broncho-pneumonia is not due to the Bordet bacillus but to streptococci, pneumococci and staphylococci as secondary invaders superimposed on the whooping-cough infection. For this reason when treating whooping cough it is always preferable to employ a mixed vaccine containing the common respiratory infecting organisms in addition to the Bordet bacillus. By this method the patient becomes prophylactically immunized to the common respiratory infecting organisms while therapeutic immunization is instituted against the Bordet bacillus infection.

The specific organism which is responsible for scarlet fever has not been determined but that the streptococcus is responsible for the serious complications which develop during the disease is well established. For this reason the use of streptococcus vaccine in this disease is logical and from the clinical results obtained, its efficiency has been demonstrated. In the natural course of the disease the temperature continues to rise until the rash begins to subside. If vaccine treatment is started early and injections made at daily intervals as a rule the temperature will come down as the rash comes out and extensive lymphangitis and other complications are avoided.

Measles is another disease in which the causative infecting organism has not been found. The disease is not serious except when pneumonia and broncho-pneumonia develop. These pneumonias are essentially streptococcus-pneumococcus-staphylococcus infections and should be treated as such by giving a combined vaccine in full dosage containing these various organisms. By this means pneumonia complications are avoided and if pneumonia has developed before the patient is brought

under treatment this vaccine treatment will materially aid in bringing about a rapid recovery.

Diphtheria is being successfully treated with diphtheria antitoxin especially when given in full dosage during the early stages of the infection, but not infrequently cases are found where the throat condition does not clear up promptly after the antitoxin is given. Such cases may safely be regarded as being due to streptococcus and pneumococcus infection in addition to the diphtheria bacillus infection. Such cases do much better when a combined pneumococcus-streptococcus-staphylococcus vaccine is given in conjunction with the diphtheria antitoxin. Really, all cases of diphtheria in which extensive involvement of the lymphatic glands of the neck is present should receive this combined vaccine in conjunction with the diphtheria antitoxin.

Typhoid fever still prevails to a large extent in some communities. That preventive inoculations with typhoid vaccine is the best means of controlling this disease is now universally recognized. In the treatment of the disease typhoid vaccine has also established itself as an efficient therapeutic agent, especially so when treatment is started as soon as febrile symptoms present themselves. Where typhoid fever is prevalent, a clinical diagnosis can readily be made during the early stages. If the vaccine is given early a permanent normal temperature may be obtained by the 12th to 15th day of the disease. In advanced cases perforation from ulcerations of Peyer's patches is recognized as being of greatest danger. There is good reason to believe that the colon bacillus, staphylococcus and streptococcus are important factors in this destructive process and to give a combined vaccine containing these organisms in conjunction with typhoid vaccine has been found of advantage.

From this brief outline of prevailing infections, it is clear that streptococci, pneumococci and staphylococci are the most persistent pathogenic agents to contend with and until this is fully realized our efforts at therapeutic immunization can only be partially successful.

BACTERIAL INTOXICATION

THE source of bacterial intoxication has long been a topic of interest when considering bacterial infections. Many theories have been advanced to explain the source of the toxins in infective processes. In infections by the so-called endotoxic organisms, like streptococci, staphylococci, pneumococci, etc., the theory that the endotoxin which is set free as a result of germ disintegration during the course of an infection received the most attention. Then, came the split protein theory which claims that during the immunizing process germs are destroyed which cause a setting free of a poisonous portion of the germ protein, and next

the proteose poisoning theory according to which bacterial intoxication is due to the absorption of the antitrypsin in the plasma by infecting organisms. All these theories fall down when investigated by animal experimentation and clinical data.

The concept that bacterial intoxication, especially in infections caused by the more common pyogenic organisms, is due to germ secreted ferments more nearly conforms to all the conditions found in infective processes and is now being more generally accepted than any other. The ferment with which the germ surrounds itself and employs to digest the food on which it lives is really the only means of defense the germ possesses and of necessity these ferments are also toxic to the tissues with which they come in contact. So when a toxic infection is encountered it is evident that the toxic irritation in the invaded tissues is due to germ secreted ferments. This is well illustrated in a case of streptococcus lymphangitis starting from a small abrasion of the skin like a needle prick such as have come under our observation and the observation of every general practitioner of large experience. Inflammatory symptoms will soon appear at the site of infection and within a day or two a chain of inflamed lymphatics will extend from the point of original infection. This shows that germ multiplication is going on rapidly and meantime bacterial intoxication is also progressing. If the streptococcus should be very virulent the case may die within 3 or 4 days. In each case it is very evident that the bacterial poisoning is most manifest along the chain of involved lymphatics. This bacterial poisoning could not be ascribed to endotoxins from dead streptococci nor from bacterial proteins derived from killed germs because there is every evidence of rapid germ multiplication and rapid germ multiplication cannot progress simultaneously in an infection with extensive germ destruction. The entire destructive process in a streptococcus lymphangitis points to the fact that the streptococci produce a toxic destructive substance during their growth and multiplication. That this destructive substance is a ferment is quite evident from our present knowledge of bacterial activities. So, when a toxic infection is encountered it should be considered in terms of germ secreted ferments which can only be relieved by eliminating the germs which are actively engaged in producing these toxic ferments. This cannot be accomplished by the application of antiseptics because any antiseptic that is powerful enough to destroy the germs will also destroy the tissues they come in contact with. Nature, however, has a better way. All living tissues possess an inherent power of self-preservation against germ invasions and this self-preservation is made manifest by ferments which these tissues produce to destroy the germs which attack them. These protective ferments are called antibodies. So, the real contest between bacterial intoxication and protection by tissue produced

antibodies is really a contest between germ produced toxic ferments and tissue produced protective ferments. If the infecting germs happen to be able to produce a very effective ferment the tissues in the infected area are destructively influenced to a point beyond their defensive ability to produce protective ferments and consequently the destructive process will be carried on to a condition of tissue necrosis, pus formation, or a fatal termination. The less virulent germs do not secrete such efficient ferments and consequently are not so toxic nor so destructive to the infected tissues. Of necessity the infected tissues are, under these circumstances, more capable of defending themselves and in a better position to produce protective ferments which have a destructive influence on the infecting organisms. Experience teaches that this reduction in virulence may be carried to a point of actually killing the germs and by injecting them under the skin, tissues so treated will be as actively if not more actively aroused in antibody or protective ferment formation than they are when brought under the influence of living germs of the less virulent types. This is the foundation on which prophylactic and therapeutic immunization rests. For prophylactic purposes, killed germs are injected into healthy tissues to train and induce these tissue cells to produce protective ferments to prevent infections by germs of the same kind as those contained in the bacterial vaccine. For therapeutic purposes killed germs of the same kind as those responsible for the existing infection are injected into healthy tissues to train and induce these tissue cells to produce protective ferments which will be conveyed from the site of vaccine injection to the infected area to there aid the involved tissues in destroying the infecting organisms.

THE ADVISABILITY OF GIVING VACCINES ON A CLINICAL DIAGNOSIS

IT IS obvious that in the application of bacterial vaccines a diagnosis is necessary. Many well-meaning physicians contend that in the interest of scientific treatment, since vaccine therapy is specific in action, a bacterial diagnosis should always be made before giving a bacterial vaccine. From a superficial consideration, this position looks reasonable but it will not bear careful analysis. Science is classified knowledge so arranged that it is capable of application for the greatest good. In treating disease, the aim is to restore health in the shortest possible time with the least suffering and the lowest mortality rate. Before any procedure in the treatment of infectious diseases can be regarded as scientific, all the factors that enter into the possibility of attaining this end must be taken into account.

When diphtheria antitoxin first came into use, being a specific treatment, it was thought necessary to verify the clinical diagnosis by a bacterial examination before its administration. Such practice is now known to be dangerous because a bacterial diagnosis will cause enough delay in treatment to prevent obtaining the best result and frequently is directly responsible for a fatal termination.

Here the combined knowledge that diphtheria antitoxin is harmless, although the case may not be diphtheria, and that early treatment is of great advantage, makes its administration on a clinical diagnosis more scientific than when used after a bacterial examination because all the facts in the situation have been considered.

The same principle applies in the administration of bacterial vaccines. In many cases of acute infection, delay in giving the vaccine may prolong the course of the disease or hazard the life of the patient. Practically all users of bacterial vaccines in the treatment of pneumonia are agreed that their earliest possible administration gives the best results.

Clinical pneumonia is not always caused by the pneumococcus. It may be primarily due to the streptococcus, Friedlander bacillus, influenza bacillus or other organisms, but here it should not be forgotten that dangerous cases of pneumonia are either due to the pneumococcus or streptococcus and frequently to a mixed infection of these two dangerous organisms. Where we have a serious pneumonia following epidemic influenza, pneumococci and streptococci coming in as secondary invaders are almost invariably the dangerous factors. This same condition applies to the Friedlander bacillus pneumonias and other pneumonias. By taking all these facts into consideration, it is certainly more scientific to give a combined pneumococcus streptococcus vaccine and preferably also one containing the other common respiratory infecting organisms (Formula 38) at once than to delay treatment for a bacterial examination, because at all events by this method the dangerous infecting organisms in clinical pneumonia are guarded against. If there were any clinical or experimental evidence to show that the immunizing mechanism is in the least interfered with by including the streptococcus in the vaccine when used in a pure pneumococcus infection, the objection would be valid. But on the contrary, we find that better results are obtained with a combined vaccine than where a single organism vaccine is employed. This may be accounted for on the ground that in addition to the immunizing response, a greater leukocytosis is obtained with a mixed vaccine than from single organism preparations.

In puerperal sepsis the streptococcus is pre-eminently the dangerous infecting organism, while staphylococcus, colon bacillus and other infecting organisms may also be factors. To overcome a streptococcus infection of this character, early treatment is absolutely essential to obtain

the best results. A bacterial examination of the blood or uterine contents would not benefit the patient's opportunity to cope with a streptococcus infection, but the immediate administration of a streptococcus vaccine would. Should no streptococcus infection be present absolutely no harm could be done. Furthermore, by giving a mixed vaccine, having in addition to the streptococcus other organisms corresponding to a probable mixed infection present, the patient will receive the immunizing benefit against these infections without in the least interfering with the streptococcus immunization from the streptococcus contained in the vaccine. This is the scientific method for treating these cases because it most nearly meets the immediate necessary requirement in handling the case.

In the application of vaccine therapy, a diagnosis which takes into account the existing infecting organisms as shown by clinical symptoms is very essential and in this connection it should be remembered that but a comparatively small variety of germs cause the bulk of diseased conditions met with, and that they usually gain entrance to the body by way of the mucous membranes. Of these the pneumococcus, streptococcus, colon bacillus and staphylococcus are the most important.

In the respiratory tract, the pneumococcus, streptococcus, staphylococcus, micrococcus catarrhalis and Friedlander bacillus form the important group, while in the digestive tract, abdominal viscera and pelvic organs, the colon bacillus, streptococcus, pneumococcus and staphylococcus are found the usual disturbing factors. From this it should be clear that by using a combined vaccine which conforms to the organisms present in the abdominal viscera and pelvic organs, most of the infectious diseases met with can be taken care of. In addition to this, we must consider that when specific infections like measles, whooping cough, influenza, or tuberculosis involve the respiratory tract and gonorrheal infection the pelvic organs, the group of infecting organisms mentioned above are usually found as complicating factors in the specific infection.

Skin infections are most frequently due to staphylococcus with the streptococcus a frequent associate.

Rheumatisms are due to the same organisms that involve the respiratory tract or abdominal viscera. By associating these various facts, bacterial vaccines may be scientifically applied to better advantage in most instances than where they are used on a bacterial diagnosis only, but from this it should not be inferred that bacterial examinations should not be resorted to. Many times a bacterial examination is the only means at our command to determine the nature of an infection, and where the case does not progress favorably such examinations should always be made while the stock vaccines indicated by clinical symptoms are being used.

The statement may be made, although it follows as a matter of course, that surgical interference, local treatment, drainage and other general measures and supportive treatment should be carried out along with the administration of any bacterial vaccine. The vaccine stimulates the immunizing mechanism and naturally cannot take care of surgery, etc., where indicated.

DOSAGE AND SITE OF INOCULATION IMPORTANT

CONSIDERABLE opposition to the use of bacterial vaccines has been encountered, especially in the treatment of acute infections, due to improper concepts of dosage based on theoretical grounds. In no field of therapeutics is proper dosage of greater importance than in therapeutic immunization. The grave mistake has been made of placing the toxic element of a bacterial vaccine to the forefront. The thought that bacterial vaccines are really given in very small non-toxic doses has not received enough attention. The average hypodermic adult dose really amounts to less than 0.0004 of a grain, of killed germs, containing an infinitesimal amount of germ toxin as compared to the toxic material already present in a case of extensive acute infection. The thought is advanced that in a case of an extensive acute infection the patient is literally saturated with bacterial toxins and consequently would require small doses of vaccines if at all given on the theoretical contention that in such cases giving bacterial vaccines would simply add more bacterial toxin to an overloaded system. This is absolutely wrong as shown by clinical experience. On the contrary, the initial dose in acute toxic infections, to obtain the best clinical results, should be three or four times larger (1.0 c.c. of Sherman's standard suspensions) than the initial dose in a subacute or chronic infection (0.2 c.c. of Sherman's standard suspensions) and the dose should be repeated at daily or twice daily intervals whereas in chronic cases injections should be made at four to seven-day intervals. Furthermore, in acute toxic infections no toxic reactions as shown by increased temperature, pulse rate or toxic nervous symptoms develop that can be attributed to the vaccine. Instead of this, if the vaccine is given reasonably early during the course of the infection, all these toxic symptoms will begin to subside in a large majority of cases within twelve to twenty-four hours with a distinct tendency to a rapid recovery and especially so if the vaccine injections are continued at proper intervals. These clinical results are so striking, when vaccines are used during the early stages of acute infections, that there can be no doubt as to their immunizing influence. The opposition to the use of bacterial vaccines in acute toxic infections is based primarily on the contention that immunization results from antibody or protective ferments which are produced by the lymphatic internal organs due to the presence of

bacterial toxins. From the fact that extensive toxic infections usually run a prolonged course or have a fatal termination, it is evident that the lymphatic internal organs are not readily influenced for antibody formation by bacterial toxins and it is also evident that the minute amount of bacterial toxin injected in the form of a vaccine could have no material influence on the lymphatic internal organs in the presence of extensive bacterial intoxication due to an infection. That the tissues at the site of the bacterial vaccine injection produce antibody as Wright contends, is much more probable. We do know that tissues at the site of vaccine injection change in respect to their tolerance to the vaccine. If vaccines are repeatedly injected into approximately the same area much less local reaction or inflammation will develop from a vaccine injection in this than in other portions of the body, showing that a distinct immunologic change has developed in these tissues as compared to other tissues of the body. It has also been found that better therapeutic results are obtained if a new area is selected for each vaccine injection. In compliance with this thought many doctors, when giving large doses of vaccine, divide the dose and make the injection in three or four different parts of the body so that a correspondingly larger area of tissues is brought under the vaccine influence. Some very excellent results are claimed for this method, especially when employed in advanced dangerous infections. It has also been found that it is better to make the injection remote from the infected area. If, for example, we have an abscess or lymphangitis in an arm, it is not advisable to inject the vaccine into that arm. When this thought, that antibodies or protective ferments are produced by the tissues into which the bacterial vaccines are injected, once becomes thoroughly fixed in a doctor's mind, he will find little difficulty in finding his way through the practical application of therapeutic immunization.

All infections are acute before they become chronic and the severe acute toxic infections like pneumonia, erysipelas, lymphangitis, sepsis, mastoiditis, scarlet fever, etc., are the most dangerous and for that reason a thorough knowledge of the proper dosage in this class of cases is most important because if bacterial vaccines are properly applied here, the most brilliant results will be obtained. Early treatment is of paramount importance because tissues into which the vaccine is injected respond much more readily for antibody formation during the early stages of an infection than after the body cells have become fatigued from bacterial poisoning for several days or a week. The attending physician should be prepared to give the proper vaccine at the first visit. The adult dose should be 1.0 c.c. and in severe cases the dose should be repeated at 12-hour intervals until the toxic symptoms subside. In the less toxic cases the vaccine may be given at daily intervals. After the temperature becomes normal and stays there, inoculations should be made at 2 to 3

day intervals until all signs of infection have subsided and to prevent a possible relapse, the vaccine should be given at weekly intervals for several weeks after a clinical recovery.

In acute minor infections with no fever like a cold, inoculations should be made at one to two-day intervals starting with 0.2 to 0.5 c.c. and gradually increasing the dose to 1 c.c. In these cases it is also important to give a few doses at weekly intervals to guard against a possible relapse.

In the treatment of acute infections we find every degree of severity from the cases without fever to the most severe cases of bacterial intoxication so the doctor must discriminate in the dosage and intervals employed to conform to the requirements of the case under treatment. The general practitioner, being accustomed to observe clinical symptoms, soon acquires the necessary information to gauge the dosage properly.

In chronic infections, we are confronted with a condition in which the infecting organism has developed a sort of tolerance for the protective substances of the body and the body tissues have also developed a tolerance to the infecting organism. To get rid of an infection thus entrenched, a highly developed immunity is required which can only, as a rule, be acquired by persistently repeating inoculations. These chronic cases are less tolerant to vaccine injections than the acute ones and consequently it is advisable to start treatment with small doses to avoid unnecessary reactions. The dose should be so gauged that a red spot at the site of injection will develop within a day or two about the size of a silver dollar. Usually, 0.2 to 0.3 c.c. will suffice for the initial dose. The dose may then be increased by 0.1 to 0.2 c.c. with each subsequent inoculation until the dose is worked up to 1 c.c. As a rule inoculations are repeated at 4 to 7 day intervals and it is found that the reaction at the site of injection decreases under increasing dosage. Where the patient is very tolerant to the vaccine, the dose may be worked up to 2 c.c. In these chronic infections, it is of utmost importance that the treatment be continued until the case is cured if it takes 6 months, a year or more. This is especially true of chronic arthritis, neuritis, asthma, cystitis, acne, etc. If a focus of infection is found, it should be removed surgically if possible, the vaccine being used at the same time to hasten the recovery. In chronic infections unusual organisms are frequently present. This can readily be determined by making a bacterial examination. In some cases an autogenous vaccine gives better results than a stock and on the other hand stock vaccines often effect a cure where autogenous vaccines have failed. In some cases very large doses, 2 to 3 c.c., given in 3 or 4 different parts of the body, followed by slight chill and fever will cause a favorable reaction which is followed by marked clinical improvement.

The vaccine should not be used intravenously because the reactions caused by this method of injection are too severe and dangerous. Just as good results, though not quite as spectacular, are obtained from the subcutaneous injection of vaccines and this method is absolutely harmless.

Infants and children tolerate vaccines very well and should receive one-quarter to one-half the adult dose.

THE NEGATIVE PHASE

THE fear of the so-called Negative Phase in applied therapeutic immunization has been largely responsible for otherwise well-informed physicians hesitating to employ bacterial vaccines in cases where they really would be of great service. Theoretically, the negative phase is a state of depressed or negative resistance to infecting organisms for several hours or more after a vaccine injection, during which time it is believed an existing infection, especially during the acute stage, may gain such headway that it will become difficult to bring the infection under control.

That such a negative phase develops from overdosing with tuberculin in the treatment of tuberculosis is well known and was the cause of abandoning the tuberculin treatment in cases of tuberculosis soon after Koch's tuberculins came into use. A negative phase also manifests itself at times in the treatment of chronic infections due to streptococci, staphylococci, pneumococci, and other organisms. Here the symptoms produced by the infection become aggravated by overdosage or by giving the vaccine at too short intervals. For this reason it is always necessary when treating chronic infections, to start treatment with a small dose to gauge the individual's susceptibility to the vaccine, and then work up on the dosage in accord with the requirements of the case under treatment. To do this effectively requires clinical experience in vaccine therapy. Since the phenomenon of a negative phase does make its appearance in the vaccine treatment of chronic infections, it has been thought that such a state would of necessity be liable to assume dangerous proportions if vaccines were employed in extensive acute infections, and especially so if the infection had assumed such proportions that the life of the patient was in the balance as it were. We can readily see how reluctant anyone with this viewpoint in mind would be to give a bacterial vaccine in a critical case of acute infection. To have a severe acute infection assume an additional virulence, if only for a few hours, would certainly be a serious affair because the headway made during this time might be sufficient to seriously handicap the patient's ability to cope with the infection during the entire course of the illness. But theoretic considerations, in a

proposition as complicated as immuno-production proves itself to be in the course of an infection, bring us nowhere. The only reliable way this proposition can be efficiently worked out is by clinical application and by applying clinical tests, we find exactly the opposite of these theoretical contentions to be true. We find that no negative phase as indicated by a rise of temperature, increased pulse rate or unusual extension of the infected area develops after a vaccine injection when given in severe acute infections even under initial doses 4 to 5 times as large as those usually employed when starting treatment in chronic infections and repeating the injections at 12 to 24-hour intervals instead of 3 to 7-day intervals as found advantageous in treating chronic infections. Furthermore, instead of a negative phase developing with a prolonged illness, toxic symptoms soon begin to subside.

Why this tolerance to large doses of bacterial vaccines, (no negative phase in cases of extensive acute infections being produced) prevails may be difficult to explain, but since efficient immunizing responses, as shown by the favorable clinical results, can only be obtained by giving these large doses it is evident that the infective conditions in these acute infections are such that large doses at short intervals are required to bring out a proper immunizing response. That in acute infections excessive toxic materials are produced and that these toxic materials do not adequately stimulate immuno-production is evident since a large amount of toxic material is present; it is also evident that a large amount of antibody is required to neutralize this toxic substance and clinical experience shows that only by giving large doses at short intervals can this be accomplished. So, to properly keep up adequate antibody formation, it is necessary to repeat large doses of vaccines at short intervals.

FOCAL REACTIONS AND RELAPSES

A FOCAL reaction in vaccine therapy is shown by a temporary clinical manifestation of increased irritability of the infected area and if such a reaction does develop after injecting a dose of vaccine, it is regarded as being of diagnostic value, it indicating that the infection is due to organisms identical to those contained in the vaccine.

Many attempts to explain these focal reactions have been made on the theory of an anaphylaxis. Dr. W. Ford Robertson in his recent book on Therapeutic Immunization regards this anaphylaxis theory of focal reactions as absolutely unfounded. He shows that instead of being an anaphylaxis, it is simply a condition in which the patient is particularly intolerant to bacterial toxins. It is not an unusual experience to have a patient who is very intolerant to bacterial toxins—persons who get severe reactions from exceedingly small doses—develop focal reactions

at the site of every previous vaccine injection as manifested by a distinct redness and infiltration of the previously injected tissues. In protein anaphylaxis, this reaction becomes worse under repeated injections whereas under bacterial vaccine injections, this reaction becomes less under continuous treatment. This shows that instead of an anaphylaxis to the bacterial protein contained in the vaccine, a tolerance to the bacterial toxin contained in the vaccine is developed as the principal factor in focal reactions. It is this deficiency of resistance to bacterial toxins, especially the toxins produced by the more common infecting organisms like streptococci, pneumococci, and staphylococci, that is responsible for many ailments not ordinarily recognized as being due to infection.

In the treatment of cases that are particularly sensitive to bacterial vaccines, we find that very small doses must be employed at first and then be gradually increased in accord with the resistance which develops. As a rule in such cases, very little therapeutic results will be observed until sufficient resistance has been developed so that an average dosage will be well tolerated. This shows that there is a close relationship between tolerance of bacterial toxins and immunity. This may be explained by considering bacterial toxins as substances that are destroyed by ferments or antibodies which are formed as a result of vaccine inoculations. So in the end, this question of tolerance would really consist of the ability to readily destroy these bacterial toxins.

Theoretically, it would appear that after an infection has once been subdued by induced antibody formation as a result of vaccine injections, that the antigenic influence of the infecting organisms still present in the infected area, would be sufficient to complete the immunizing process and eliminate the infection; but from clinical experience, we find that this is not the case. It is a common experience to find, while treating cases of pneumonia, erysipelas, puerperal sepsis, typhoid fever, etc., that after giving several doses of vaccine and material improvement has developed, that if the vaccine treatment is then discontinued, in a large percentage of cases, the infection will again take on new activities which will again subside if vaccine treatment is reinstituted but unfortunately not infrequently, this renewed activity of the infection will not respond as adequately to the vaccine treatment as when the infection was first brought under control. This in all probability is due to the infecting organism, as time goes on adapting itself to its environment, immunizing itself to the antibody formed by the body cells, so that it becomes more and more difficult to destroy the infecting organism by the immunizing process. For this reason it is always advisable, when treating acute infections, to continue the vaccine treatment until the infection is entirely eliminated and also to give a few more doses during convalescence.

To summarize: The negative phase plays no part in the treatment of acute infections. The best therapeutic results are obtained by giving large doses at short intervals. To obtain permanent results vaccine treatment must be continued until the patient is completely convalescent.

RELIEF FROM PAIN UNDER THERAPEUTIC IMMUNIZATION

DURING his early work in therapeutic immunization, Wright demonstrated that with the development of an immunity during an infection, we also simultaneously obtained relief from pain. This is particularly noticeable in cases of acute infections under vaccine treatment. This is well illustrated in cases of lobar pneumonia. The pain of lobar pneumonia is characteristic. As a rule a person coming down with pneumonia suffers sufficiently to call a physician, soon after the initial chill. If vaccine treatment is started soon after the initial chill by giving a full dose of a combined pneumococcus-streptococcus-staphylococcus vaccine, it will be found that relief from pain will be observed within 18 to 24 hours and if the vaccine injections are continued at daily or twice daily intervals enough immunity will be developed to abort the infection in a large majority of cases with complete relief from pain. What is true of pneumonia, is also true of acute streptococcus infections of wounds or tonsils, otitis media, etc.

This relief from pain under therapeutic immunization is readily explained from what is known in immunologic science. That the severe pain at the site of an acute infection is caused by the irritating effect of the germ produced toxins or ferments, which the germ employs to digest the food on which it lives, is apparent. That other manifestations of pain, headache, aching pains throughout the body, etc., are due to germ-produced toxins that have been conveyed throughout the body from the infected area is also clear. Evidently, one of the first functions of an antibody, whether produced as a natural consequence in overcoming an infection, or as a result of vaccine inoculations, is to neutralize this germ-produced toxin or ferment. It is by means of this ferment, that the germ employs to digest the food on which it lives, that it defends itself against phagocytic action. If antibody is formed which neutralizes this germ-produced ferment, of necessity the toxic irritation will be eliminated and thereby relief from pain will be established. This would apply to the ferments that have permeated the entire body as well as those present in a more concentrated form at the site of infection. These germ-produced ferments are not only irritating to the tissues but to the phagocytes as well and as long as a germ is capable of surrounding itself with an active digestive ferment, phagocytes find such a germ too toxic for attack

and consequently we have no phagocytosis, we have what is known as a negative chemotaxis. These antibodies, however, by neutralizing the ferment surrounding the germs, reduce the offensive character of the germ sufficiently to allow phagocytic action. Consequently this antibody does not only function by eliminating the toxic, germ-produced substances but also indirectly causes germ destruction.

There is really nothing more characteristic in immuno-therapy than this relief from pain after vaccine injections. In pneumonia cases, it is found that under daily injections of vaccine even in advanced cases, relief from pain is a characteristic symptom and will serve a better purpose in quieting a restless patient than morphine without producing harmful depressing effects which so often follow the administration of a narcotic. What is true of pneumonia also holds good with other acute infections under vaccine treatment.

LIVE VIRULENT GERMS ARE NOT DEPENDABLE ANTIBODY PRODUCERS

SPONTANEOUS recovery from an infectious disease is due to the development of an immunity. Prolonged infections are due to retarded immunization. Virulent, live bacteria in an active infection often inhibit immunization, resulting in a fatal termination. It is this tendency of live bacteria in an active infection to retard or inhibit immunization that makes the infectious diseases so dangerous. Killed or devitalized bacteria, when injected under the skin, rapidly stimulate antibody production. This is clearly demonstrated from our experience with prophylactic vaccine inoculations.

It is the realization of this fundamental principle, that live virulent bacteria have a tendency to retard or inhibit immunization while killed bacteria inoculations readily stimulate antibody production, that justifies the application of vaccine inoculations in the treatment of acute infectious diseases.

Where the virulence of bacteria has such a devitalizing influence on the tissue cells with which they come in contact that antibody production is retarded or inhibited, enough healthy tissue can always be found into which vaccines may be injected for the purpose of "getting them busy" in antibody production and in this way aid the diseased tissues in overcoming the acute infection.

TONIC EFFECT OF VACCINES

TONIC properties are ascribed to many measures; but, generally speaking, any agent that aids in building up the vitality of the body may be considered a tonic. This implies increased healthy metabolism

with increased cell activity. Many measures in common use have this stimulating effect, among them wholesome outdoor exercise, sunlight, properly applied hot and cold baths, massage, electric radiation, mental composure, etc.

Vaccines are primarily regarded efficient as immunizing agents in the treatment or prevention of infections; but, from clinical observation, we find that this does not limit their field of usefulness. One of the most constant and characteristic results, following the use of vaccines, especially when applied in the treatment of chronic infections, is the rapid development of a feeling of well-being associated with a keen desire to take food, good digestion and an increase of body weight. Here is evidence of increased cell activity, augmented healthy metabolism, which can only be ascribed to the vaccine injections and should be regarded as a tonic influence.

This tonic influence of vaccines has not received the attention it deserves. Tonics in all probability exert their influence by stimulating cell activities through a certain kind of cell irritation. The tonic property of arsenic is probably due to cell irritation and the same may be said of other tonics. One of the most common experiences is the development of robust health after recovering from an infectious disease, even by those who are not so vigorous before the illness. Recoveries from typhoid fever are illustrative. This may be best accounted for on the ground that, as a result of the infection, tissue cells have been stimulated to renewed activities and that these activities, after being once acquired, will continue up and beyond the requirements of eliminating the infection, which culminates in increased constructive metabolism. Cell activities, which result from vaccine injections, are identical with those obtained from eliminating an infection; but since the injection of killed germs are incapable of doing any harm, the benefits of these tonic activities may be obtained without the danger incidental to an infection. That these vaccine injections do arouse cell activities identical to those which develop by overcoming an infection is easily determined by compliment deviation tests, the opsonic index, agglutination tests, blood counts, etc.

This general tonic effect of vaccines may be applied to advantage in any case where other remedies fail. It is usually advisable to use a colon bacillus combined vaccine for this purpose.

REFERENCE TO FORMULA BY NUMBER

IN order to avoid the tedium of a useless repetition of formulæ as the occasion of mention demands, the formulæ have been referred to by number. The formula number and the formula following it is given in the following tabulation:—

LIST OF SHERMAN'S BACTERINS

Sterilized Without Heat

Acne Combined Vaccines

33	Acne Bacillus	40,000,000
	Staphylococcus Albus	1,000,000,000
50	Acne Bacillus	40,000,000
	Colon Bacillus	300,000,000
	Staphylococcus Albus	1,000,000,000

Catarrhal Combined Vaccines

40	Streptococcus	100,000,000
	Pneumococcus	100,000,000
	Micrococcus Catarrhalis	200,000,000
	Staphylococcus Aureus	200,000,000
	Staphylococcus Albus	200,000,000
36	Friedlander Bacillus	300,000,000
	Micrococcus Catarrhalis	200,000,000
	Pneumococcus	100,000,000
	Streptococcus	100,000,000
	Staphylococcus Aureus	200,000,000
	Staphylococcus Albus	200,000,000

Colon Bacillus Combined Vaccine

(*Modified Van Cott*)

35	Streptococcus	100,000,000
	Pneumococcus	100,000,000
	Staphylococcus Aureus	300,000,000
	Staphylococcus Albus	300,000,000
	Colon Bacillus	200,000,000

Erysipelas Vaccine

1	Streptococcus Erysipelatis	100,000,000
	Staphylococcus Albus	200,000,000

Gonococcus and Combined Vaccine

25	Gonococcus	1,000,000,000
49	Gonococcus	1,000,000,000
	Streptococcus	100,000,000
	Pneumococcus	100,000,000
	Colon Bacillus	200,000,000
	Pseudo-Diphtheria B.	300,000,000
	Staphylococcus Albus	1,000,000,000

Influenza Bacillus Combined Vaccine

38	Influenza Bacillus	200,000,000
	Streptococcus	100,000,000
	Pneumococcus	100,000,000
	Micrococcus Catarrhalis	200,000,000
	Staphylococcus Aureus	200,000,000
	Staphylococcus Albus	200,000,000

Meningococcus Vaccine

34	Meningococcus	1,000,000,000

Pneumococcus Combined Vaccine

6	Streptococcus	100,000,000
	Pneumococcus	100,000,000
	Staphylococcus Aureus	200,000,000
	Staphylococcus Albus	200,000,000

Staphylococcus Combined Vaccine

22	Staphylococcus Aureus	1,000,000,000
	Staphylococcus Albus	1,000,000,000

Streptococcus and Strepto. Combined

42	Streptococcus	400,000,000
10	Streptococcus	120,000,000
	Staphylococcus Aureus	300,000,000
	Staphylococcus Albus	300,000,000

Tubercle Bacillus Vaccines (Non-virulent)

45	Non-virulent T. B.	500,000,000
47	Non-virulent T. B.	1,000,000,000

Typhoid and Combined Vaccine

30	Typhoid Bacillus	1,000,000,000
46	Typhoid Bacillus	1,000,000,000
	Paratyphoid Bacillus "A"	750,000,000
	Paratyphoid Bacillus "B"	750,000,000

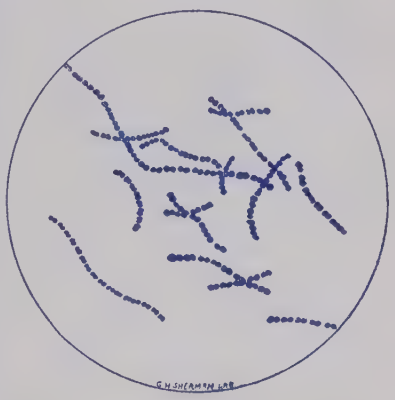
Whooping Cough Vaccines

37	Bordet's Bacillus	3,000,000,000
43	Bordet's Bacillus	3,000,000,000
	Micrococcus Catarrhalis	100,000,000
	Pneumococcus	40,000,000
	Streptococcus	30,000,000

BACTERIOLOGY

Of the more common Pathogenic Organisms.

Streptococcus



THE Streptococcus is a parasitic pathogenic organism. The cells are spherical and are usually united in chains, of varying lengths, due to the division of the organism in one plane only. Under certain conditions it may be aggregated in irregular heaps or masses. It is non-motile and does not form spores.

The hemolytic streptococcus is one which causes destruction of hemoglobin in the blood.

The streptococcus viridans causes a green discoloration of the blood when grown on artificial culture media.

The non-hemolytic strains have little effect on blood culture mediums.

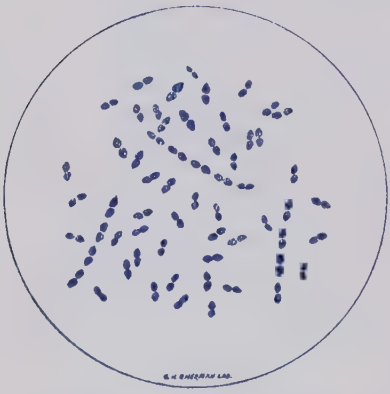
Sherman's streptococcus vaccine contains a representative selection of these various strains.

The streptococcus occurs not infrequently in the various orifices and in the alimentary canal of healthy individuals. Such organisms are to be regarded as potentially virulent and pathogenic in all cases.

Streptococci may be primary pathogenic invaders, or they may be secondary invaders whose activities complicate, modify and sometimes outweigh in importance those of the primary invaders. They are found in tonsillitis, rheumatism, erysipelas, malignant endocarditis, periostitis, otitis, meningitis, pneumonia, empyema, lymphangitis, sepsis, puerperal endometritis and many other forms of inflammation and septic infection. In man, invasion by the streptococcus is usually associated with active suppuration and sepsis.

The suppurative conditions for which the streptococcus is held to be responsible, differ from those caused by the staphylococcus in having a greater tendency to spread, and are more prone to generalized infection or septicemia.

Pneumococcus

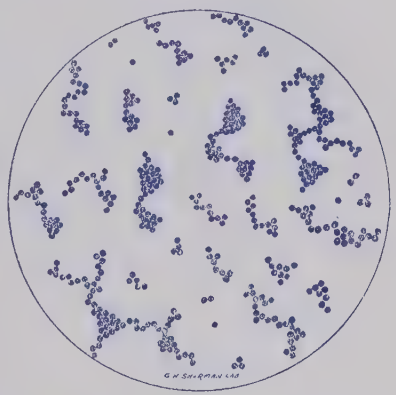


THE typical pneumococcus is a small slightly elongated coccus, conical or lance shaped, which shows a marked tendency to occur in pairs (diplococci) with the broader ends in opposition. Occasionally it is arranged in short chains resembling the streptococcus. All pneumococci except a few strains are enveloped by a capsule. Since there is an unusually high mortality attending infection with the pneumococcus mucosus, or type III, which has a well developed capsule, it has been suggested that the capsule may protect the organism against the injurious influence of the body fluids.

Pneumococci are divided into four groups (Types I, II, III, and group IV). The most severe types of pneumonia are produced by Types I, II and III. Type I is often found in cases of lobar pneumonia. The types of organisms in group IV are variable in their pathogenic power. All four types of the organism are found in Sherman's pneumococcus vaccine.

The pneumococcus is not only held responsible for most of the cases of lobar and broncho-pneumonia, but also for a large number of other pathological conditions. It is commonly found in the inflammations of the pleura, pericardium, endocardium and sometimes the meninges. Practically all body tissues are subject to attack by this organism. It may also be found in middle ear infections, abscesses, empyema, suppuration in the antrum, purulent arthritis and in acute and chronic catarrh.

Staphylococcus Pyogenes Aureus



THE staphylococcus is one of the most common pathogenic bacteria, usually present on the skin and mucus membrane, and is the organism commonly found in boils, furuncles, ulcers, eczema and abscesses, and similar suppurative inflammations. Infection by this organism is usually localized, and frequently produces copious quantities of pus. Primary infection by this organism is often followed by lowered resistance and repeated reinfection.

The cells are small and spherical occurring solitary, in pairs as diplococci or in groups of four but most commonly in irregular masses, similar to clusters of grapes. The staphylococcus aureus stains readily and is gram positive, non-motile, aërobic, facultative anaërobic micrococcus. Grows readily on all culture media. It liquifies gelatin. On agar the growth is whitish at first, later becomes a rich golden yellow on the surface. The yellow pigment is produced only in presence of oxygen. Milk is coagulated. Acid, but no gas, is produced in media containing carbohydrates.

The staphylococcus has greater resistance to outside influences, heat, sunlight, dessication, etc., than other non-spore bearing pathogenic bacteria. The pathogenic effect of the staphylococcus aureus on test animals varies considerably as to application, virulence of culture employed and species of animal used.

Staphylococcus Pyogenes Albus

THIS organism is found primarily on the skin, in certain types of acne as a primary factor and in others in symbiosis with the Bacillus Acne. It is also found as a complicating factor in various types of urethritis.

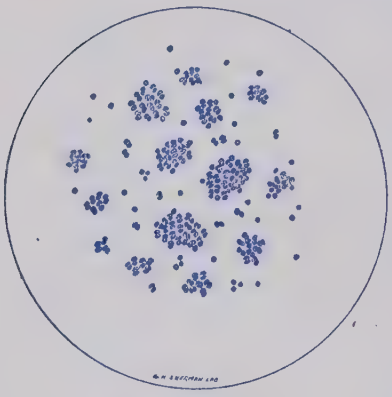
It is morphologically identical with the aureus, and is considered by some to be the same organism which has lost the property of producing pigment. Surface cultures on all media are white. The Biological characteristics can not be distinguished from staphylococcus aureus.

Staphylococcus Citreus

THIS organism is seldom found in the pus of acute abscesses, but occasionally is found associated with other pyogenic cocci and is distinguished from the other staphylococci only by the formation of a lemon yellow pigment.

If cases of staphylococcus infection do not respond promptly to inoculations of albus and aureus vaccine, it is advisable to have a bacterial examination made to ascertain if the staphylococcus citreus is responsible for the infection.

Micrococcus Catarrhalis

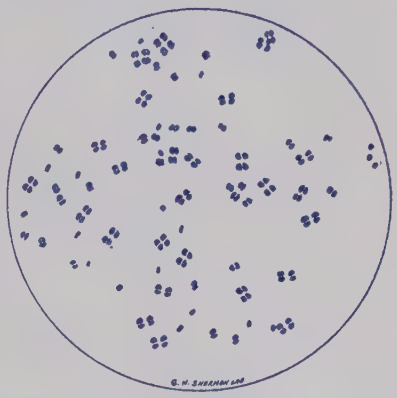


THE micrococcus catarrhalis is spheric or slightly ovoid. It may occur singly, though usually in pairs or clusters. It is readily taken up by the leukocytes and may resemble the gonococcus or meningococcus.

It is found in the sputum, nose and throat, in cases of bronchitis, pneumonia, whooping cough, colds, bronchial catarrh and other affections of the respiratory tract.

Owing to the frequent occurrence of this organism in the upper respiratory tract, it may be mistaken for the meningococcus. It may be differentiated by the fact that it does not ferment dextrose and maltose as does the meningococcus.

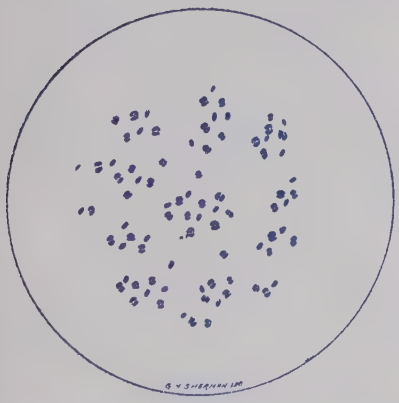
Meningococcus



THE meningococcus occurs as diplococci in groups within the leukocytes. In culture it occurs as cocci, diplococci and tetrads. There are four types or varieties of meningococci which are distinguished by their agglutination reaction.

This organism causes cerebrospinal meningitis. It may also produce hemorrhagic septicæmia without meningitis.

Gonococcus



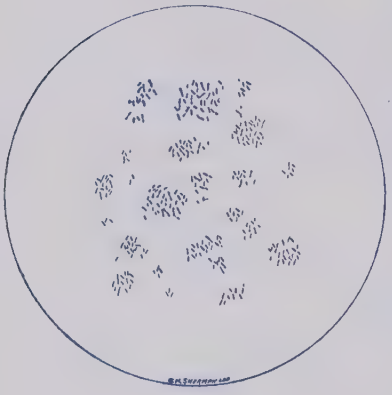
GONORRHEA, which is confined to the human race, is one of the most prevalent of bacterial diseases. It is met with throughout the civilized world. The causative organism was first demonstrated by Neisser, in 1879, but was not cultivated on a culture media until 1885.

Gonococci usually occur in pairs with the adjacent sides flattened and separated by a small interval so that they resemble a coffee-bean. They are non-motile, non-sporing and are not stained by Gram's method. In preparations made from gonorrheal pus, the organisms are found within the pus cells, very few ever lying free. For isolation they require nutrient agar containing blood, blood serum or ascitic fluid at a temperature of 30° to 38° C. They die readily at room temperature and are very sensitive to light and drying.

The most frequent seat of infection by this organism is the genito-urinary tract but it also commonly causes conjunctivitis, arthritis, and endocarditis. Occasionally a septicæmic condition may occur. In rare

cases meningitis is caused by the gonococcus in which case great care must be taken to distinguish that organism from the meningococcus which it resembles in appearance. The gonococcus does not grow on ordinary culture media unless a considerable quantity of pus is smeared on the surface.

Influenza Bacillus



THE influenza bacillus is one of the smallest pathogenic organisms. It is non-motile and non-sporing but the poles have a tendency to stain more deeply than the center. It occurs singly, in small groups, threads or in short chains. Hemoglobin is essential for the growth of this bacillus.

The organism is found in abundance in the secretions of the mouth and nose of "influenza" patients. Mixed infections of the influenza bacillus with the pneumococcus or the streptococcus are frequently encountered. The invasion of the body is through the air passages.

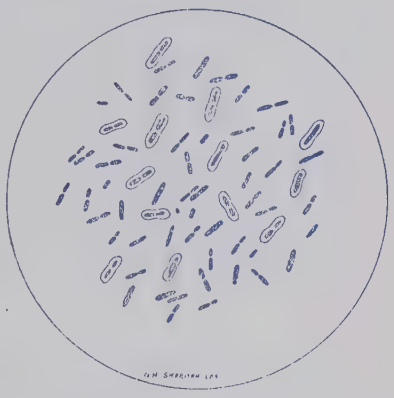
When lung tissue is affected, a lobular type of pneumonia is the result. It is sometimes found in inflammation of the middle ear and of the meninges.

Bordet Gengou Bacillus (Bacillus Pertussis)

THIS Bacillus, the cause of whooping-cough, is a short, oval rod, variable in size, non-motile, and gram negative. It is aërobic, facultative anaërobic; when first isolated in pure culture it grows best upon glycerin-potato-blood-agar. Later generations grow more or less copiously upon the ordinary culture media. The bacillus is isolated from sputum with difficulty. The first week of the disease offers the best opportunity for isolation. As the disease progresses it becomes increasingly difficult to isolate the organism.

This Bacillus can be differentiated from the influenza bacillus and other organisms closely resembling it, which are present in the sputum of whooping-cough cases by its growth *without* the presence of hemoglobin in the culture medium.

Bacillus Friedlander



B. FRIEDLANDER was at one time regarded as the cause of Lobar Pneumonia. The bacillus varies from coccoid forms to the longer bacilli which are often surrounded by a wide capsule. It grows freely on ordinary media, characteristically mucoid with a tendency to confluence. This organism at times is the cause of both broncho and lobar pneumonia.

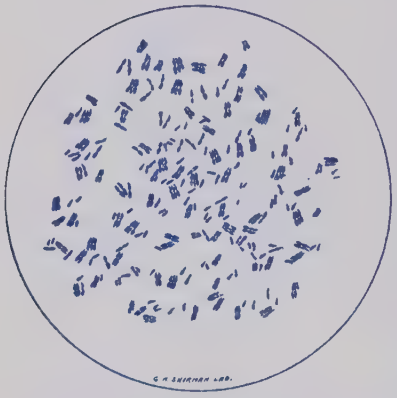
This type of pneumonia has a high mortality, the bacillus is often present in the sputum, sometimes in almost pure culture. The bacillus is commonly present in the upper respiratory tract and the accessory sinuses, where it causes inflammation or infection of ear, eyes, and nose.

It is found most frequently in cases of ozena or fetid catarrh.

Bacillus Acne

THE acne bacillus is a short, rather plump, irregularly club-shaped bacillus, occurring in acne pustules and comedones. It is non-motile, gram positive and takes ordinary stains readily. Pure aërobic cultures are difficult to obtain. It grows best with only a small amount of oxygen. In the deep-indurated types of acne, other organisms, such as the staphylococcus, play an important role.

Bacillus Hoffmann
(*Pseudo Diphtheria Bacillus*)



THIS Bacillus is found in the nose, throat, eye and other parts of the body. It bears some morphological resemblance to the diphtheria bacillus; its growth is also similar.

It is rather short, plump and more uniform in size and shape than the true Löffler bacillus. In young cultures when stained by the Neisser method, it shows no polar granules, and stains evenly throughout with methylene blue. No acid is produced by the fermentation of glucose, as in the case of a virulent diphtheria bacillus.

When these organisms are found in cultures from cases of suspected diphtheria they may lead to an incorrect diagnosis.

Bacillus Typhosus

THE typhoid bacillus is a short cell, rather plump and rod shaped, having rounded ends and often grows into long threads. It stains with the ordinary anilin colors, and is gram negative. The typhoid bacillus is motile when living under favorable conditions. It often has numerous flagellæ, which spring from the sides as well as ends. Many short rods have but a single terminal flagellum. The bacillus grows well on all sugar free media and resembles the B. colon, but grows somewhat slower and not quite so luxuriantly.

Acid and gas is produced in mannite, maltose and dulcite is acted upon after prolonged incubation. Acid, but no gas, is produced from dextrose, galactose and levulose. Milk is not coagulated. It is impossible to produce typhoid fever in animals except the anthrapoid apes.

Typhoid bacilli freshly obtained from typhoid cases will not produce the disease when introduced subcutaneously in animals. In typhoid fever, during the early stages, the bacilli pass to all parts of the body, and become localized in certain tissues. In typhoid fever, as in other infectious diseases, toxic poisoning may be manifested by disturbances in the circulation, and respiration as well as by manifest lesions. In a few cases the intestinal lesions are absent. The most practical test for early diagnosis of typhoid fever is the blood culture and later the Widal or Agglutination reaction.

Para Typhoid A

The Para Typhoid A. Bacillus produces a typhoid-like disease in man, most frequently encountered in the warmer areas. The bacillus may be present in the feces, urine, blood and bile.

The Para Typhoid A. Bacillus is similar to the typhoid bacillus in many respects. It does not, however, produce acid from Xylose. It is communicable, the same as typhoid. Not all strains are alike in their agglutination reaction.

Para Typhoid B

This type is considered to be distinctly pathogenic to humans, therefore different from similar paratyphoid types found in animals. If this is correct, the infection by B. paratyphosus "B" is transferred only from man to man. Clinically, the Para Typhoid B. infection resembles typhoid fever. Morphologically, the bacillus closely resembles the other members of this group but grows more freely and rapidly. Diagnosis is determined by agglutination tests.

Colon Bacillus

THE colon bacillus has a variable morphology. The typical form is that of short rods with rounded ends but sometimes the rods are so short as to be almost spherical. They occur as single cells or sometimes as pairs joined end to end. The most typical of the colon group possess motility.

There is a question as to whether the colon bacillus is always virulent or whether it becomes so under abnormal conditions. In some of the intestinal diseases such as typhoid, cholera and dysentery the bacillus seems to

acquire an increased virulence at the same time, and easily finds its way into the general system causing suppurative lesions where it is thus absorbed from the intestines. It frequently enters the kidney causing inflammation and nephritis, or it may invade the bile duct leading to inflammation, obstruction, suppuration, or calculus formation. It may be the cause or complicating factor in cholera infantum, endocarditis, meningitis, liver-abscess, broncho-pneumonia, pleuritis, chronic tonsillitis, urethritis, appendicitis, cystitis and peritonitis.

Tubercle Bacillus

THE tubercle bacillus is a slender non-motile rod-like organism with an average length of about one-half the diameter of a human red blood cell. The bacilli occur singly or in pairs, and are usually slightly curved, branching and club-shaped forms may also be observed.

Owing to a waxy substance, the bacillus does not readily take up the ordinary anilin colors but when once stained it is very difficult to decolorize, even by the use of strong acids, therefore it is called an acid fast organism.

It grows best at a temperature of 37° C. It is very resistant to both heat and drying. Because of its purely parasitic qualities it does not multiply outside the living body.

The tubercle bacillus is pathogenic not only for man but for a large number of animals; such as the cow, monkey, pig, cat, etc.; young guinea pigs are very susceptible and are used for detection of tubercle bacilli in suspected material.

ABSCESSES

ABSCESSES are formed as a result of tissue necrosis at the point of a submerged infection. They are most commonly due to staphylococci, streptococci, colon bacilli or a combination of two or more of these organisms as a mixed infection. Drainage in these cases is essential. Bacterial vaccines to hasten immunization are very useful in that immunization hastens repair and thus avoids the formation of a chronic fistula. Formula 35 or 10 are the proper combinations to be employed in these cases. Inoculations are made at one to three day intervals, depending upon the severity of the infection, one c.c. inoculations being employed at daily or two day intervals in severe cases and smaller doses at longer intervals in the less severe.

ACNE

ACNE divides itself into two classes of cases. The pustular form, in which the pustules are superficial, and the nodular form, in which comedones predominate.

In the pustular variety the staphylococcus albus is the infecting organism and in this class of cases good results are being obtained with staphylococcus vaccine. Some doctors use a vaccine containing the staphylococcus albus only, but generally a combined staphylococcus aureus and albus vaccine (Formula 22) is preferably employed. This being a chronic condition, it is best to start treatment with a small dose 0.2 c.c., gradually increasing the dose as indicated by the clinical results and reactions at the site of inoculation. If within a day or two, an infiltrated area, at the site of inoculation, develops greater than the size of a silver dollar, the dose has been larger than necessary, indicating that the subsequent dose should not be materially increased or possibly made slightly smaller. As treatment is continued there will be less infiltration under increasing dosage, and after four or five injections there may be no material reaction after giving 1 c.c., but from this it should not be inferred that the dosage must be continually increased to obtain therapeutic results. As a rule it is not necessary to go beyond 1 c.c., but occasionally a case is found where it is necessary to work up the dose to 2 c.c. It is also important not to make the injections at too short intervals. Generally, given 3 to 7 days apart is sufficient. Persistency in treatment, however, is of great importance. In most of the cases marked improvement takes place soon after starting treatment, while others progress slowly, but if the treatment is persistently carried out this class of cases will get better if necessary local treatment is also applied. Where deep-seated pustules exist they should be lanced, and the pus evacuated and local antiseptics employed to take care of surface

infections. Hot applications and other measures to stimulate the circulation of the skin and hasten absorption of indurated tissues are employed to advantage.

In acne vulgaris of the nodular variety, where the skin is filled with comedones, the acne bacillus is regarded as the chief pathogenic factor. The organism is a difficult one to isolate and grow, and for this reason autogenous vaccines are seldom prepared from the acne bacillus, nor do they appear to be of any advantage where they have been employed. Autogenous vaccines are sometimes prepared from the staphylococcus found in acne infections and a stock acne bacillus vaccine added to the suspension.

Most physicians preferably employ the acne bacillus combined with the staphylococcus albus in the vaccine, and there is no good reason why the two organisms may not be advantageously used together in a vaccine.

There is some difference of opinion on dosage in the use of acne vaccine; some recommending large doses, but most observers cling to the small dose in starting treatment and working up. There have probably been more failures in the treatment of acne with acne vaccine from overdosing than from not giving enough. The negative phase is an important factor in the treatment of acne with acne bacillus vaccine. Focal reactions in the skin lesions are common from overdosing. Treatment is usually started with 5,000,000 to 8,000,000 acne bacilli (0.1 to 0.2 c.c. of Formula 33). If three to six or more new pustules develop within 24 to 48 hours after the injection, the dose has been too large. The next dose, then, should not be repeated until the reaction has entirely subsided and conditions appear to be at their best, which may be anywhere from the fourth to the tenth day after the inoculation, but usually about the fifth or sixth day. Where no material reaction follows an inoculation, as shown by new pustule developments, the dose may be increased by one to three millions for the next inoculation. The dose may be worked up to 40,000,000 or more. The staphylococcus albus vaccine is given in the usual small dosage at first and the dose is gradually increased to 1,000,000,000 or more.

The importance of proper dietetics and the necessity of taking care of digestive disturbances in the treatment of acne has long been recognized. In the presence of digestive disturbances the addition of the colon bacillus to the acne staphylo combined vaccine is a distinct advantage. Formula 50 is admirably adapted for this purpose. It contains Acne Bacillus 40,000,000, Colon Bacillus 300,000,000, and Staphylococcus Albus 1,000,000,000 per c.c. In persistently chronic cases a combined colon-strepto-pneumo-staphylo vaccine (Formula 35) used alternately at 3 to 5 day intervals with an acne staphylo combined vaccine, will often bring results where the other vaccines have failed.

The local care of the lesions is of utmost importance in obtaining the desired results, and care should be taken that this treatment is applied at the proper time. Soon after giving the vaccine the patient passes into the negative phase. This lasts about two days, and during this time no local treatment should be employed, because any kind of irritation during this time has a tendency to aggravate matters. Two days after an inoculation the patient passes into the positive phase, and for about two days careful attention should be given to local measures. The patient is directed to then apply hot moist applications, press out comedones and manipulate the skin to increase the blood supply to the infected foci. Gasoline carefully applied with absorbent cotton naturally aids in softening the crusted ends of the comedones, when they can be readily pressed out. Pustules that make their appearance should be opened and where possible the attending physician should do this. These pustules are often deep-seated and should be opened. The pustules should never be cauterized with carbolic acid or other chemicals that have a destructive influence on the tissues, because such treatment will cause unsightly scars and pits.

Persistence in the use of the vaccines and local care of the skin are the essentials in procuring ultimate success. Apparently hopeless cases, relapsing after temporary improvement, by continuing the treatment for six months or a year as a rule ultimately get well. For this reason it is never wise to abandon a case, even if no material improvement is observed in the first few months treatment.

ACCIDENTAL WOUNDS[1]

ADENITIS

ACUTE lymphatic gland inflammation is usually due to streptococcus infection from a focus of infection adjacent to the involved glands. Staphylococcus complications are very frequent. In throat conditions the pneumococcus also often plays a part. So a combined streptococcus, pneumococcus, staphylococcus vaccine (Formula 6) is preferably employed. In cases with considerable fever treatment should be started with 0.5 to 1. c.c. and injections repeated at one to two day intervals until the infection has subsided and at 3 to 5 day intervals during convalescence. In very severe cases the vaccine should be given at 12 hour intervals.

APHTHÆ[2]

APPENDICITIS

IN this serious inflammatory condition a mixed infection usually prevails in which the colon bacillus, streptococcus, pneumococcus or staphylococcus are the most important infecting organisms. Immediate

[1]See Wounds
[2]See Mouth Infections

measures for rapid immunization toward controlling the infection are of utmost importance to guard against post-operative extensions of the infection and to aid in procuring a rapid recovery. Formula 35 is admirably adapted for this purpose. The attending physician should administer the vaccine at the first indication of an appendicular infection and meantime the advisability of an immediate operation should not be neglected. Where the infection has progressed to the production of fever 1.0 c.c. dosage of the vaccine should be employed, and injections made at 1 to 2 day intervals until the fever has subsided and at 3 to 5 day intervals after that until convalescence is complete.

ARTHRITIS[1]

ASTHMA

ASTHMA is caused by a sensitization to various forms of protein dust such as dust from feathers, fuzz, horse hair, the various pollens, flower, grain, etc., and from the irritation caused by the various bacteria which are responsible for respiratory infections. The streptococcus, pneumococcus, and staphylococcus are the most common and are frequently associated with the micrococcus catarrhalis, influenza and Friedlander bacilli. The tubercle bacillus is an important factor in some cases. Even in cases where the asthma is primarily due to dust or pollen sensitization germ invasions by these respiratory infecting organisms are material factors in aggravating the asthma. So therapeutic immunization with bacterial vaccines will even benefit these cases. The asthmas due to repeated attacks of bronchitis, which eventually become chronic, however, constitute by far the larger proportion of asthmatic cases that present themselves for treatment. As a rule these cases are very susceptible to "taking cold" and every time they get an attack of acute coryza the infection in the bronchi becomes worse, resulting in an aggravation of the asthmatic condition.

That bacterial vaccine inoculations have a marked therapeutic value in bronchial infections is now well established and in these asthmatic cases it is found that improvement usually takes place soon after giving the vaccine. Mixed infections being the rule, a combined bacterial vaccine should be employed. Formula 36 or 38 is the combination that is most extensively used. Treatment is started with about 0.2 c.c. or 3 minims and the dose gradually increased to 1 c.c. or more. Inoculations should be made at from three to seven-day intervals. Where severe asthmatic symptoms exist, the usual drugs employed to give temporary relief should be used in conjunction with the vaccine. The vaccines, however, as a rule, will soon have enough influence so that medical sedatives become unnecessary.

[1]See Rheumatism

Extremely chronic cases often require treatment over a long period of time, for 6 months or more and not infrequently cases that have recovered will relapse with the first "cold" they contract. In these cases the vaccine treatment must be renewed and vigorously carried out. In time these "colds" with the asthma will cease to relapse.

BLEPHARITIS MARGINALIS

THIS chronic infection of the margin of the eyelids if not directly due to coccus infections is at least complicated with staphylococci, and often with streptococci. The results obtained immunologically from the use of staphylococcus and staphylococcus, streptococcus combined (formula 22 or 10) vaccine would confirm the relationship of these organisms to the disease. Very obstinate cases have been cured by this method. Dosage and interval between inoculations should be the same as in other minor localized infections, i.e. start treatment with 0.3 c.c. of vaccine and repeat inoculations at 3 day intervals, increasing dosage as indicated by local reaction, which should not be greater in area than a silver dollar.

BLOOD INFECTIONS

INFECTIONS of the blood are not uncommon. After germs have gained entrance to the blood stream and maintained themselves for several days immunity to get rid of them does not develop until the infection localizes in the tissues of some part of the body. The idea that if the blood is infected that the infection has invaded the entire body is erroneous. In these cases the great bulk of the body tissues are not infected; so the infection is not general. The streptococcus, pneumococcus and staphylococcus are the most common organisms capable of growing and multiplying in the blood. Wright calls such organisms serophytes.

In the early stages of blood infections bacterial vaccines are very efficient. By injecting killed germs under the skin, a condition is produced imitating localization of the infection, local tissues being involved. These tissues become actively engaged at the site of vaccine injection in antibody formation, which, when absorbed by the blood will sufficiently reduce the virulence of the infecting bacteria in the blood to make phagocytic activity effective for their elimination. This beneficial effect of bacterial vaccines is particularly noticeable when they are given early in cases of puerperal sepsis, and the septicemia following wound infections, relief from toxic symptoms with reduction of temperature often taking place within 24 to 36 hours. Early treatment being of paramount importance, treatment should not be delayed to make a bacterial diagnosis but in the puerperal cases a mixed vaccine preferably also

containing a colon bacillus (formula 35) should be given in 1.0 c.c. dosage repeated at 12 to 24 hour intervals until the fever has subsided, when the injections may be extended to 3 or 4 day intervals until recovery is complete. In other forms of blood infections from infected wounds, etc., formula 6 or 10 may be employed to advantage.

BOILS[1]

BONE INFECTIONS[2]

BRONCHITIS

BRONCHITIS prevails as an acute or chronic affliction. It is very common and in the acute condition is usually regarded as a "cold on the chest" and often appears in epidemic form. The various types of pneumococci and streptococci are the most constant and most dangerous organisms present. Staphylococci, the micrococcus catarrhalis, influenza and Friedlander bacilli are also common invaders in these acute bronchial infections.

In the treatment of these cases a mixed vaccine is usually employed. Formula 40 meets the most common prevailing condition. If the influenza bacillus is present formula 38 is preferable. The presence of the Friedlander bacillus calls for formula 36. In acute bronchitis treatment is started with the usual small dose, 0.3 c.c. and then increased by 0.2 to 0.3 c.c. with subsequent injections in accordance with the amount of reaction which develops at the site of inoculation. Severe cases with fever should receive larger doses than those without fever and inoculations are made to advantage at one to two day intervals. By this prompt and persistent treatment the bronchial infection will usually subside within three or four days and infrequently will last more than a week or ten days. After the more acute symptoms subside inoculations should be made three or four days apart and should be continued until all symptoms of bronchial infection have disappeared.

In chronic bronchitis we find the same organisms present that prevail in acute cases. Occasionally we find a case in which the colon bacillus is present with two or more of the other organisms. These cases usually have a foul breath. Cases with a chronic Friedlander bacillus infection also have a disagreeable odor and an expectoration which is inclined to be very copious. In chronic cases the same vaccines are employed as in the acute cases. Treatment is started with the usual small dose 0.2 or 0.3 c.c. and the dose gradually increased to 1 c.c. or more, inoculations being made at 4 to 7 day intervals, in cases showing the greater amount of reaction the interval between injections being longer. Formula 40 or 38 is preferably employed. In cases of Friedlander bacillus infection, formula 36 is necessary and in cases where the colon bacillus is present, formula 35 is used.

[1]See Furuncles.
[2]See Osteomyelitis.

The results from the use of bacterial vaccines in chronic bronchitis are uniformly good. It being a chronic infection, it takes longer to effect a symptomatic cure than in the acute cases and relapses when epidemics of "colds" prevail are common. By persistent treatment, however, an immunity is gradually developed which becomes lasting with a resulting recovery.

BRONCHO-PNEUMONIA[1]

BURNS

A BURN is essentially a wounded skin, subject to infection by the staphylococcus and streptococcus. Much of the pain and burning sensation which develops after the initial pain subsides, which was caused by the burn itself, is due to infection of the burned area. By proper immunization with bacterial vaccines the pain due to this infection is relieved. A staphylococcus-streptococcus combined vaccine, formula 10, when given at one or two day intervals in dosage proportionate to the severity of the infection will serve the best purpose.

CARBUNCLES[2]

CEREBRO SPINAL MENINGITIS

CEREBRO SPINAL MENINGITIS is most commonly caused by the meningococcus, but occasionally we have cases due to streptococci, pneumococci or influenza bacilli. This can be determined by bacterial examination of the cerebro-spinal fluid procured by lumbar puncture.

In Meningococcus meningitis, antimeningococcus serum should be given intra-spinally. It has been found that meningococcus vaccine given hypodermically in conjunction with the serum treatment is of great advantage. Formula 34 should accordingly be given in 1 c.c. doses at daily intervals until the meningeal symptoms have subsided and at 3 to 4 day intervals during convalescence. If the meningitis should prove to be due to other organisms, a corresponding vaccine should be employed in 1 c.c. doses at daily or twice daily intervals.

The prophylactic use of meningococcus vaccine is promising and should be employed in all cases exposed to meningococcus infection. Three or four injections of 1 c.c. of formula 34 should be made at 5 to 7 day intervals.

CHOLECYSTITIS

GALL bladder infection is usually due to the common pyogenic infecting organisms, streptococci, staphylococci, pneumococci and the colon bacillus predominating. Formula 35 is here indicated. The dosage conforms with that used in subacute and chronic infections. Treatment is started with 0.2 or 0.3 c.c. and then gradually increased to 1 c.c., making

[1]See Pneumonia.
[2]See Furuncles.

inoculations at 4 to 7 day intervals. Unless there is obstruction from gallstones, liver symptoms will soon subside with a restoration of the normal functioning of the liver.

COLDS[1]

REPEATED bacterial examinations of the minor respiratory inflammations commonly called "colds," have conclusively demonstrated that these ailments are due to infection and that virulent strains and types of streptococci and pneumococci are the chief infective agents with staphylococci, micrococcus catarrhalis, Friedlander and influenza bacilli as common complicating agents.

Most of us are bothered with these respiratory infections at various times, particularly during the winter months. To tolerate a cold until it "wears off" is the prevailing method of treatment. The average person does not consult a doctor for the treatment of colds because he is not yet aware that prompt relief can be obtained by the vaccine treatment.

These respiratory infections often run a prolonged course because the infecting organisms irritate the mucus membranes too severely to actively stimulate them for rapid antibody formation. In fact, the infection entirely too often lapses into a chronic condition. By injecting killed germs, like the ones responsible for the infection, in vaccine form in a remote part of the body, antibodies are produced by the tissues into which the vaccine was injected. By means of the circulating medium these antibodies are conveyed to the infected mucus membrane and there aid in overcoming the infection. A polyvalent mixed vaccine (formula 40, 38 or 36) should be employed.

In these minor acute infections with little or no fever, treatment should always be started with a small dose about 0.3 c.c. of the standard suspension; not because large doses are dangerous, but because unnecessary uncomfortable reactions are liable to develop if treatment is started with a large dose. The dose should be gradually increased to 1.0 c.c. and inoculations made at 1 to 3 day intervals.

Usually within one or two days after the first inoculation, the acute symptoms subside, and if the inoculations are then repeated at 3 to 5 day intervals for several more injections to prevent a relapse, recovery will soon be complete.

Much has been said of late about the advantages of prophylactic vaccination against pneumonia. The results so far obtained show this to be entirely practical, but most people are not inclined to take prophylactic injections for a disease that appears to be a remote possibility. This is entirely different, however, when one has a cold. By curing the cold with vaccine, we at the same time prophylactically immunize ourselves against pneumonia. We have never known a case of pneumonia to develop where

[1]See also Rhinitis.

the preliminary cold was treated with vaccine. Colds are the forerunners of other serious infections, such as mastoiditis, sinusitis, nephritis, arthritis, endocarditis, etc. If the primary respiratory infections are treated with vaccine, enough immunity will be established to prevent the later complicating infections.

COLITIS

INFLAMMATORY conditions of the colon are due to the same pyogenic organisms which prevail in gall-bladder infections, and the same vaccine is used in these cases.

CONJUNCTIVITIS[1]

CORNEAL ULCER[1]

CYSTITIS

THE bacteriology of cystitis has been extensively studied, and it appears that in about 60 percent of the cases the colon bacillus is the primary cause. In many cases, however, other organisms come in as secondary invaders, especially the staphylococcus, streptococcus and pneumococcus. The pseudo-diphtheria bacillus, bacillus pyocyaneus and Friedlander bacillus are found in some cases. The gonococcus in cases of gonorrhea is also frequently present. A specimen of urine procured under aseptic precautions with a catheter makes a ready means of procuring a culture for bacterial examination.

A colon bacillus vaccine does not give as satisfactory results in these cases as a mixed vaccine, even if no other organisms but the colon bacilli are found. Observers on the use of vaccines in cases of cystitis are quite unanimous that this is the best method of treatment, but many contend that while the clinical symptoms indicate a cessation of the inflammatory condition and urine examinations show a great reduction in the number of germs, in a majority of cases the germs do not entirely disappear. For this reason, the vaccine treatment should not be discontinued after inflammatory symptoms subside. Treatment should be continued to build up a high degree of immunity. Being a subacute or chronic condition treatment should be started with the usual small dose 0.2 or 0.3 c.c. of Formula 35 and the dose gradually increased to 1 c.c. or more, making inoculations at 4 to 7 day intervals. In cases of gonorrhea, the gonococcus should be included in the vaccine. If other organisms are present as shown by bacterial examination, a corresponding stock vaccine should be used or an autogenous vaccine should be prepared.

[1]See Eye Infections.

DACRYOCYSTITIS[1]

DERMATITIS

DERMATITIS is due to infection of the skin by the ordinary skin organisms, the staphylococci predominating. Staphylococcus vaccine Formula 22 is employed to good advantage in these cases. "Prickly heat" or chafing during hot weather where the skin becomes irritated from excessive perspiration is really due to a lowered resistance to staphylococcus activities. Staphylococcus vaccine given at 5 to 7 day intervals is very effective in these cases. Impetigo is also due to infection by the ordinary skin organisms assuming an extensive, acute form and should be treated with staphylococcus or staphylo-strepto combined vaccine Formula 22 or 10. Injections are made at 2 or 3 day intervals.

DIABETES

THAT diabetes is due to a suspension of the secretion of a sugar metabolizing substance by the pancreas or more particularly that portion of the pancreas containing the islands of Langerhans has recently been conclusively demonstrated by the discoveries of Dr. Banting and his co-workers in the University of Toronto of Canada. They extracted a substance from the pancreas which they called Insulin that serves the purpose of metabolizing the sugar contained in the blood of diabetics when administered hypodermically. This shows that the pancreas is an internal secreting organ as well as performing the function of secreting the pancreatic fluid which is employed in intestinal digestion.

The suspension of the internal secretion of the pancreas can be accounted for as being the result of an infection which interfered with the function of the organ. This is verified by the fact that pancreatitis is commonly associated with diabetes. Whether the use of Insulin in cases of diabetics will restore the health of the patient sufficiently to overcome this infection of the pancreas must be determined by extensive clinical investigation. At all events, if the infection has gone on to a point of actual destruction of this pancreatic internal secreting function, no restoration of the function can be expected, even if the infection subsides. In that event, it would be necessary to continually supply the insulin much the same as thyroid extracts are being supplied to cases of cretinism.

Since diabetes is evidently due to an infection of the internal secreting portion of the pancreas, our first aim should be to get rid of the infection. (See "Pancreatitis as Related to Gastro-Intestinal and Gall Bladder Infections"—Seale Harris, M. D., Birmingham, Ala., J. A. M. A., Nov. 3, 1923., P. 1496.) Unless the infection is extremely acute, an organ may be infected for a considerable length of time before the function of the organ is destroyed. Pancreatic infections apparently are not of the extreme

[1]See Eye Infections.

acute type. There is always a period during which the function of the pancreas can be restored if the infection is relieved. Furthermore, there are many cases of diabetes in which the infection of the pancreas has only extended to a point of partially suspending the internal secreting function so by relieving the infection the pancreatic function is readily restored.

That the immunizing method by means of bacterial vaccine injections is the best method for eradicating infections and restoring normal functioning of infected organs is now generally admitted. That this applies to diabetes is a matter of clinical experience where vaccines are applied reasonably early, before the function of the pancreas has been irreparably destroyed by the infection. As a rule, a decrease in the amount of sugar in the urine with an increase of the general health condition is observed within a few weeks after starting treatment. To avoid overtaxing sugar metabolism, a diabetic diet should be adhered to until it is found that more sugar and starches can be assimilated and where indicated Insulin should of course also be administered. Eventually, the urine will become sugar free and allow of a return to normal diet. In early cases, such results will be obtained within two or three months. If the infection has progressed to an actual destruction of the internal secreting function, no restoration of this function can be expected. Since it is impossible to know just to what extent the infection has progressed, it is always advisable to give the patient the benefit of the doubt by giving the vaccines. Many advanced cases will materially improve, even if they are not entirely relieved, showing that some portions of the insulin secreting function of the pancreas are restored so a moderate diet of sugar and starch can be taken care of.

In selecting a vaccine for administration, we must realize that the pancreas is subject to infection by the same pathogenic bacteria that are responsible for other acute and chronic abdominal infections. Of these, in the abdominal viscera, streptococci, colon bacilli, staphylococci and pneumococci are the most common and mixed infections by two or more of these organisms are the rule. It would appear logical to give a mixed vaccine such as Formula 35 which contains these organisms. Being a subacute or chronic infection, treatment is started with 0.2 or 0.3 c.c. and the dose gradually increased to 1 c.c., making inoculations at 5 to 7 day intervals. If not much reaction develops at the site of injection, the dose may be rapidly increased to 1 c.c. or more.

Many cases of diabetes are subject to furunculosis and boils. In such cases, it is well to give a staphylococcus vaccine, Formula 22 alternately with 35, at 3 or 4 day intervals until the furunculosis has disappeared.

This vaccine treatment is entirely harmless and will not interfere nor conflict with the insulin or any other treatment, and may be employed in any stage of the disease in children as well as in adults, children receiving proportionately smaller doses.

DUODENITIS[1]

EAR INFECTIONS

UNDER ear infections it is well to include infections of the external auditory meatus, because they are usually classed as ear diseases. Of these, furunculosis is the most important. Furuncles of the auditory canal are particularly painful and often run a prolonged course when immuno-therapy is not employed. The offending organism in the less severe types is usually the staphylococcus albus, while in the more severe types, the staphylococcus aureus is found. These cases yield readily to combined staphylococcus aureus and albus stock vaccines. If treatment is started early, before a necrotic center with pus formation has developed, the infective process can be aborted, with a resulting rapid recovery. Where the infection is farther advanced, the immunizing influence of the vaccine will relieve the pain, and the swelling will subside, with a resulting small abscess which can be readily drained and healed. Full sized doses of staphylococcus vaccine (Formula 22) should be given by starting treatment with 0.5 c.c. and working the dose up to 1 c.c. or more within three or four inoculations. Injections should be made two or three days apart for the first two or three doses, and five to seven days apart thereafter for three or four weeks, so as to build up an immunity and prevent a recurrence.

Acute otitis media is practically always due to an extension of the infective process from the naso-pharynx through the Eustachian tube and naturally is due to the same organisms found in infections of the pharynx. The streptococcus and the pneumococcus have a more distinct tendency to infective extension than other organisms found in the nose and throat, and for this reason are most frequently found in acute middle ear infections. The Friedlander bacillus, the micrococcus catarrhalis and the influenza bacillus, are also found. After there is an opening through the ear-drum, staphylococci, by migration from the auditory canal, gain entrance to the middle ear and in time the staphylococcus often overgrows and displaces the original infecting organisms so that the staphylococcus may be the only organism found. In cases of chronic suppurating otitis, various organisms like the bacillus pyocyaneus, the colon bacillus, the pseudo-diphtheria bacillus, and the bacillus proteus are frequently found and occasionally we find typhoid or tubercle bacilli.

In the treatment of suppurating otitis with vaccines, it is necessary to take this difference in the bacterial flora of the early acute stages and the chronic conditions into account. In the acute conditions, early treatment is of great importance, both as a means of relieving pain and to avoid destructive and dangerous extensions of the infection. One of the first

[1]See Gastro-Intestinal Infections.

symptoms of otitis is pain in the ear. When an earache is associated with an acute infection of the naso-pharynx, this is sufficient evidence that the infection has extended to the middle ear and if a vaccine has not been given for the existing "cold," it should be employed at once for the ear complication. If there is a bulging of the drum, it should be lanced, but if the infection has not advanced sufficiently to cause much fluid accumulation in the middle ear, the early use of vaccine will in most instances abort the affection in time to avoid the necessity of opening the ear-drum. Because of the fact that streptococci and pneumococci are the principal offenders, a stock vaccine containing at least these two organisms should be employed, but the combined vaccine usually employed in the treatment of colds (Formula 40) serves every purpose. The initial dose should be about 0.3 c.c. If no material reaction develops at the point of inoculation, a somewhat larger dose should be given the next day. By this time the pain in the ear should be practically gone and inoculations at 2 or 3 day intervals with gradually increasing doses, until 1 c.c. is given, should entirely clear up the trouble within one to two weeks. Where it is necessary to lance the drum or where the drum is ruptured, it will be found that the ear dries up rapidly with a correspondingly rapid closing of the ear-drum. Where drainage through the tympanic membrane is established, cultures for bacterial examinations should be made, and if the patient should not be progressing favorably under the stock vaccines, an autogenous vaccine should be prepared.

The advantages of treating acute otitis in infants and children with vaccines deserves special mention. Local treatment in these cases is always surrounded with much difficulty and as a rule the mother or nurse finds it difficult to follow instructions, whereas a few vaccine inoculations will accomplish infinitely more, while the little patient may be allowed to go without treatment between inoculations.

In cases of chronic suppurative otitis media, the staphylococcus aureus and albus are the most frequent pathogenic factors. For this reason a combined staphylococcus aureus and albus vaccine (Formula 22) in doses of 0.5 to 1 c.c. may be given on a clinical diagnosis for several inoculations, and if prompt improvement does not take place, cultures for a bacterial examination should be made to determine the infecting organisms and a corresponding stock vaccine given, and, where unusual organisms are present, an autogenous vaccine should be prepared.

From a review of the literature on this subject, it is apparent that some cases are not benefited by vaccines even when the utmost care is employed in the selection of a vaccine and its administration. In many of these cases, there is, in all probability, some necrotic bone present in some obscure place, while in others the conditions of the tissue cells in the infected area have become such that a tolerance to the infecting organisms

has been created to a point where immunizing responses can no longer be aroused. This should emphasize the importance of always employing vaccines in the acute cases, where uniform good results are obtained, and by this means prevent the development of an unfortunate chronic condition.

Mastoiditis

THE great danger from an acute otitis is extension of the infection to the mastoid cells. When immuno-therapy is applied sufficiently early, this complication can be avoided. If the infection has already extended to the mastoid, a dose of combined streptococcus-pneumococcus-staphylococcus vaccine (Formula 6) should be given at once as an adjunct to such surgical procedures as may be necessary.

In such cases the infection is usually so extensive that 0.5 to 1 c.c. should be given, and the same dose repeated at 1 to 3 day intervals. Cultures should also be made for bacterial examination, and to provide for the possible necessity of preparing an autogenous vaccine.

The importance of therapeutic immunization in acute middle-ear infections is not sufficiently appreciated. These ear infections are too serious to allow them to progress without employing all the means at our command to stop the progress of the infection. The time to avert danger and to institute the best treatment is before the danger point has arrived. The early use of a mixed stock vaccine containing the organisms that cause dangerous mastoid infections is the safest and surest method of avoiding the development of a mastoiditis.

ECZEMA AND PSORIASIS

THE bacterial cause of eczema and psoriasis has not been established. We have made many bacterial examinations from scrapings of the skin in eczema cases but the staphylococcus aureus which is normally on the skin is the only organism found. In our early experiences with vaccines, staphylococcus aureus and albus vaccine was used in acute cases of the moist variety of eczema with excellent results. The same vaccine was used both stock and autogenous in chronic dry eczema with indifferent results.

In the acute moist cases, a staphylococcus combined vaccine (Formula 22) is given by starting treatment with 0.5 c.c. and gradually increasing the dose to 1 c.c. or more, making inoculations at 3 to 5 day intervals. As a rule, the skin dries up within a week or so. The injections, however, should be continued for several weeks at weekly intervals to prevent a relapse.

In the chronic cases—and this includes eczema of infants and children who should receive proportionately smaller doses—Formula 35 is being

successfully employed. Treatment is started with 0.3 c.c. and the dose increased by .1 or .2 c.c. to 1. or 1.5 c.c. inoculations being made at 5 to 7 day intervals. Some cases improve very rapidly while others progress slowly but steadily. In some of these obstinate cases, it has been found that giving Formula 35 alternately with Formula 22 by giving each vaccine at weekly intervals will do better than 35 alone. This will bring the inoculations 3 or 4 days apart. In some cases, it is necessary to continue the treatment for six months or more with an eventual recovery.

Psoriasis is a skin affliction in which the causative organism has not been isolated but from experience we find that the same vaccine employed in chronic eczema will also take care of psoriasis. As a whole, psoriasis cases are more stubborn, but by persistent treatment it is possible to obtain satisfactory clinical results in a large proportion of the cases treated.

EMPYEMA[1]

ENDOCARDITIS[2]

EPIDIDYMITIS[3]

ERYSIPELAS

IMMUNITY assumes two forms, local and systemic. A local immunity is manifested by the development of a local resistance to certain infecting organisms while other parts of the body, composed of the same variety of tissue are still susceptible to the infection. This is well illustrated in a case of erysipelas. Here the inflammation subsides first where the infection started, but continues to extend into new territory until it finally dies out. This shows that during the infection a localized immunity does not influence the surrounding tissues sufficiently to prevent its extension until sufficient antibody has been absorbed from the tissues in the affected area to develop a systemic immunity, when the infection can no longer extend. In addition to this localized tissue resistance, antibodies formed in any part of the body may, by means of the circulating medium, be conveyed to all parts of the body and render the entire body immune.

Of the various skin infections met with by the general practitioner, erysipelas is the most serious. That the streptococcus is the cause of the infection, is now well established. Clinical symptoms are sufficiently characteristic to enable an early diagnosis; in fact, a clinical diagnosis can, as a rule, be made in less time than a culture could be incubated and examined. From an extensive experience in taking cultures from cases of erysipelas, it will be observed that the streptococcus is not as easily found

[1]See Pneumonia.
[2]See Heart Infections.
[3]See Gonorrhea.

as might be expected. We have never isolated streptococci from cultures procured from blebs; staphylococci always being found in abundance. Cultures from pus, where an abscess developed in the deeper tissues, always showed streptococci in great numbers. Where no pus has developed, the best way to procure cultures is to make small incisions through the skin with advancing margin of the infection and then press out blood and serum from the deeper structures.

As in other acute infections, early treatment is important to procure the best results. The theoretical contention that vaccines are not applicable in severe acute infections largely accounts for the reluctance displayed by many physicians to apply vaccines in erysipelas. Some of our early experiences in the use of vaccines were in cases of erysipelas and from the results obtained there was no question concerning their therapeutic value, regardless of theoretical considerations.

A stock vaccine prepared from a number of strains, isolated from erysipelas cases, should be employed. Because of the fact that staphylococci are found in such great abundance in the inflamed area it occurred to us that this organism is a complicating factor of some importance in this disease, and accordingly we combined staphylococci with the streptococcus erysipelatis in the preparation of vaccine Formula 1. Inoculations should be repeated at daily intervals in 1. c.c. doses until the acute symptoms subside, and thereafter at 2 or 3 day intervals. If the vaccine is given before the infection has had time for spreading extensively—during the first and not later than the second day—the course of the disease will be aborted, a speedy recovery occurring. Such striking results are not secured when the vaccines are employed later in the course of the disease, but even in advanced cases marked beneficial results are obtained, unless the case is already moribund. In extremely bad cases it is advisable to give two doses of vaccine the first day, and then inject it at daily intervals for two or more days. A reduction of temperature with subsidence of toxic symptoms such as nervousness and delirium should ensue within one or two days. The inflamed area will not be so pronounced and the swollen margin not so elevated. Where pus formation has taken place, proper drainage is necessary. After the more acute symptoms have subsided, vaccine treatment should be continued at 4 to 6 day intervals for several more inoculations.

Spontaneous recovery from an attack of erysipelas often leaves the person more susceptible to subsequent attacks, showing that the live virulent organisms do not influence tissue cells for permanent immunization, but on the contrary have a tendency to break down the immunizing mechanism. If vaccine treatment is continued, however, for a month or two, making inoculations at weekly or two week intervals, an immunity can be built up which will be fairly permanent.

ETHMOIDITIS[1]

EYE INFECTIONS

IN considering the treatment of eye infections with vaccines, the question naturally arises whether immunizing substances which are developed in other parts of the body can be conveyed by means of the blood to the non-vascular structures of the eye, like the cornea, lens, vitreous, etc. It is well known that when infecting organisms gain lodgement in the tissues where immunizing substances are not readily available, the infections are liable to become destructive in character. This applies with unusual significance to the eye, in view of the importance of the organ and the amount of serious permanent damage that may follow even a small amount of tissue destruction. It does not require much of a central corneal ulcer to permanently impair vision. Let us take, for example, a corneal ulcer due to a streptococcus or pneumococcus, in a case where the immunizing resistance to these organisms is comparatively low. A corneal ulcer is necessarily too small a lesion to arouse systemic reaction enough for so much production of antibodies that an adequate amount of them will find their way to the eye and destroy the infecting organism before irreparable damage is done. But by injecting a bacterial vaccine under the skin a very large amount of tissue, as compared with that involved in the corneal infection, is actively called into service for antibody production. This antibody is then conveyed, by means of the circulatory system, to the infected cornea and aids in destroying the germs long before it would have been possible for the infection in the cornea to stimulate an equal amount of antibody production.

What is true of corneal infections applies equally to infections of other non-vascular structures of the eye. Eye infections are quite common and are met by the general practitioner almost as frequently as by the eye specialist. Early immunization being of so much importance, it is necessary that the general practitioner should familiarize himself with the bacteriology and the vaccine treatment of eye infections, because he is often called to treat these cases before an eye specialist is called into service.

Eye infections are most prevalent during the season of the year when "colds" prevail. This conforms to the popular conception that "the cold has gone to the eye" and the etiologic findings show that this conception is well grounded because the same infecting organisms which are found responsible for complications following colds are also responsible for eye infections. Of these the pneumococcus and streptococcus are the most important with the staphylococcus as a secondary invader.

[1]See Nose Infections.

This knowledge furnishes a basis for giving a combined pneumococcus, streptococcus, staphylococcus vaccine (Formula 6) as a routine in eye infections like conjunctivitis, keratitis, iritis and dacryocystitis, on a clinical diagnosis especially so because early treatment is so important. On arriving at a clinical diagnosis, however, it is very important to carefully consider a possible gonorrheal conjunctivitis or a specific iritis. In case a gonorrheal conjunctivitis or iritis should be found, gonococcus vaccine should be employed at once in conjunction with appropriate local treatment. Treatment may be started with a 200,000,000 dose of gonococcus vaccine and injections repeated at two or three day intervals, increasing the dose as indicated by reactions and clinical results. Syphilitic iritis should be treated with appropriate syphilitic measures.

The non-specific eye infections constitute by far the larger proportion of acute eye infections met with in the daily routine of practice. In these cases the combined pneumococcus, streptococcus, staphylococcus vaccine serves a very useful purpose. In conjunctivitis, keratitis, dacryocystitis and iritis marked improvement may be confidently expected within a few days and by repeating the inoculations at two to four day intervals, a speedy recovery may be confidently expected. In ulcerative keratitis, especially in children, one of the most characteristic clinical symptoms of improvement is almost complete relief from blepharospasm within one or two days after the first inoculation. The ulcer will also be found to heal much more rapidly. In dacryocystitis, the destructive character of the infection is avoided to the extent that the lachrymal sack and canal will resume their normal function and thus avoid the disagreeable condition following a constricted tear duct. Treatment in these acute eye infections is started by giving the small dose employed in other minor acute infections and gradually increasing it as indicated by the reaction and clinical improvement.

In chronic eye infections it is always advisable to make a bacterial examination, especially if marked improvement does not follow a few injections of vaccines on a clinical diagnosis, because in chronic eye infections, infecting organisms may be present that have a distinct tendency toward chronic infections, when a corresponding stock vaccine or an autogenous vaccine should be employed.

One of the annoying infections of the eye is the hordeolum. Styes are nothing more than small furuncles in the margin of the eyelids. The staphylococcus, albus and aureus are responsible for these furuncles. A combined staphylococcus aureus and albus vaccine (Formula 22) gives excellent results in these cases. The vaccine is given at three to seven day intervals and since these styes are so liable to recur, the treatment should be continued for several weeks after the furuncles have disappeared to effect a permanent cure.

FELON

A FELON is one of the more common types of painful, and from a utilitarian standpoint, important periosteal and bone infection. Many a person has a crippled thumb or finger due to this infection. Early drainage by cutting through the periosteum gives fairly good results but due to the infection, healing is frequently slow, resulting in bone necrosis. When seen early the cases can be aborted with staphylococcus, streptococcus (Formula 10) vaccine given in 0.5 to 1 c.c. doses at one to three day intervals. This vaccine is also of great advantage to promote healing after drainage has been established.

FISTULA[1]

FURUNCLES, CARBUNCLES AND BOILS

THAT drainage and local applications in the treatment of furuncles, carbuncles and boils serve a useful purpose, is beyond dispute, but to solely rely on these measures, as many physicians do, clearly shows how reluctantly new and better methods of treatment are adopted as long as the ones employed are in a measure efficient. These localized skin infections, if not as a rule serious, are certainly painful and sufficiently disagreeable to deserve the best available treatment.

That a low resistance to the staphylococcus prevails is evident from the tissue destruction and intense inflammation which develops before the infection runs its course. There is a distinct tendency for several boils to develop in succession. This shows that a systemic immunity does not develop spontaneously during recovery from a boil.

There is little difficulty in making an early diagnosis. The intensely painful throbbing localized inflammatory condition is very characteristic. As a rule, the infection is sufficiently virulent to cause tissue destruction, forming a necrotic center rather early, but characteristic of staphylococcus infections, this destructive process usually does not become extensive, but remains confined near the site of primary invasion. In this respect, staphylococcus infections differ markedly from streptococcus infections. Streptococcus infections, sufficiently virulent to cause tissue necrosis, spread rapidly and cause extensive destruction. So, when a very circumscribed intense inflammatory area of the skin is observed, it may safely be regarded as staphylococci. The therapeutic value of staphylococcus vaccine in these cases is very pronounced and for this reason, early treatment is of great advantage. If the vaccine is given before a distinct necrotic center has developed the infection can be aborted. Unfortunately the doctor does not often see these cases sufficiently early to apply the vaccine in time to abort the infection. On

[1]See Abscesses.

the other hand, during this early stage, a boil appears such a small affair that many times it is not regarded as of sufficient importance to merit a vaccine injection. This is an erroneous viewpoint. All infections start with a small beginning, and if the fact that therapeutic immunization can be most effectively carried out when applied early were generally recognized, infections would be brought under control before destructive processes would have time to develop.

When treatment is started later, after pus formation and tissue necrosis has developed, the inflammation around the necrotic center will become less angry and recede, leaving a small inflamed area in close proximity to the center of infection. Drainage will then be freer, because the surrounding tissue is not so intensely swollen, and will not encroach on the opening. In far advanced cases with several openings, with extensive inflammatory infiltration and irregular slough, vaccines are employed to advantage in that the inflammation will subside sooner and the healing process be augmented.

Wright's contention that pain and a low immunity are closely related in infective processes is well illustrated in the treatment of boils with vaccines. The infecting organisms during their life process secrete digestive ferments which are utilized to prepare the food on which they live. These ferments have a distinct irritating destructive influence on the tissues with which they come in contact and necessarily cause a great amount of pain. Germs when exposed to antibodies, lose their virulence, evidently due to the neutralizing influence that the antibody has on the digestive ferments which they secrete; consequently the destructive, irritating, pain producing property of the infection is eliminated. Relief from pain is often felt twelve to eighteen hours after the first inoculation, and, as a rule, the patient is quite comfortable in twenty-four to thirty-six hours.

Stock vaccines serve every purpose, but in the selection of a vaccine, many doctors make the mistake of employing what is known as a "mixed infection vaccine" instead of a staphylococcus vaccine, simply because the mixed vaccine, in addition to other organisms contains staphylococcus. To employ these other organisms in addition to the staphylococcus in the vaccine, can do no harm, but as a rule, the staphylococcus portion of a "mixed infection vaccine" is not sufficient to properly take care of a distinct staphylococcus infection to the best advantage. A frank staphylococcus infection, like a carbuncle, calls for a staphylococcus vaccine, and since the staphylococcus albus is sometimes present, a combined staphylococcus aureus and albus preparation (Formula 22) is preferably employed. Treatment should be started by injecting 0.5 c.c. and gradually increasing the dose to 1.0 c.c., making inoculations at one to two day intervals until the extreme acute symptoms have subsided,

and at three to four day intervals after that. The treatment should be continued for several weeks after the carbuncle has entirely healed, at weekly intervals, to build up an immunity which will prevent additional boils from developing.

In furunculosis the infection assumes a less acute form with a distinct tendency to successive crops developing. The staphylococcus aureus is the one most frequently found as the pathogenic agent, but the albus variety is also often found and calls for a combined staphylococcus aureus and albus vaccine (Formula 22).

The results from the use of staphylococcus vaccine in the treatment of furunculosis are so striking that this serves as a classical illustration to show that killed organisms are better agents to stimulate tissue cells for anti-body formation in the presence of an active infection, than the live organisms responsible for the infection. Furuncles have a distinct tendency to relapse and become chronic, new furuncles continually appearing while the old ones are healing, and this may continue over periods of months or years. Every one of these furuncles will cause more local and constitutional disturbance than a staphylococcus vaccine inoculation, still one dose of vaccine will stimulate more antibody production, as shown by the clinical results, than that developed from the combined influence of all the furuncles, extending over a period of months or years.

Every physician is familiar with the obstinate character of these cases under medical and local treatment; especially their tendency to relapse. Furunculosis cases usually present a condition in which all stages of furuncles may be seen, some healing, others fully developed, some partly developed, or just starting. This gives a good opportunity to study the aborting effect of staphylococcus vaccine. The fully matured furuncles, after being drained, will heal rapidly, the partially matured will become less active and heal rapidly after being lanced, while those that are just starting will generally subside. Treatment should be started with the usual small dose, 0.3 c.c., and increased as indicated by clinical improvement. Inoculations are preferably made at three or four day intervals, until the infection is brought under control and at five to seven day intervals after that—for at least one or two months—to prevent relapses. For this purpose, large doses are sometimes necessary, it being generally advisable to work the dose up to 2.0 c.c. of Formula 22 before discontinuing treatment.

GANGRENE[1]

GASTRO-INTESTINAL INFECTIONS

THE colon bacillus frequently becomes a pathogenic organism in the alimentary tract, instead of restricting its activity to feeding upon the fecal masses. It is then a pus producer, infecting the intestinal walls

[1]See Wounds.

with a resulting colitis, duodenitis, appendicitis, proctitis, etc. The consequences of these alimentary infections may manifest themselves in practically any portion of the body; it is well known that acne, eczema and other skin disturbances may have an enteric basis. An ascending infection into the gall bladder may take place, with a resulting cholecystitis or cholangitis. Nor does it fail to make its way into the genito-urinary organs, causing cystitis, pyelitis, nephritis and the like. The frequency of intestinal disturbances in cases of chronic rheumatism indicates a causal relationship.

Generally the colon bacillus is accompanied by other pus producers found in the mouth and swallowed, streptococci, pneumococci and staphylococci. In gastric ulcers for example, the streptococcus is practically always present. Duodenal ulcers have a similar bacterial flora. In colitis streptococci and staphylococci also play an important role. So when selecting a vaccine in the treatment of these cases a combined vaccine containing all these organisms should be selected (Formula 35 serves this purpose). Treatment should be started with the usual dose 0.3 c.c. and gradually increased to 1 c.c. or more, making inoculations at 5 to 7 day intervals. The tonic influence in addition to its immunizing action is a decided advantage, in these cases. This tonic influence increases the appetite, which is always a good symptom to those suffering from gastro-intestinal infection. Proper diet and regulation of the bowels of course is necessary.

GONORRHEA

WHEN treating gonorrheal infections it is important to realize that the gonococcus is an organism which has a distinct tendency to produce subacute and chronic infections and is very slow in building up an immunizing resistance. This has been clearly brought out by applying the complement fixation test as a means of determining the presence of a gonorrheal infection; complement fixation being obtained only in cases where gonococcus antibodies have developed to measurable proportions. These complement fixation tests show no positive reactions from cases of anterior urethritis or vulvo-vaginitis. A posterior urethritis may show a positive reaction during the sixth week. Positive reactions may be obtained in about fifty per cent of prostatic cases. From this we must infer that extensive deep-seated gonorrheal infections are necessary to produce a measurable amount of antibody. It is also found that immunities produced by the gonococcus are of short duration. Recovery from an attack of gonorrhea offers no protection to a subsequent attack. In fact a second gonorrhea is often more intractable than the first infection.

As a result of the early conceptions of vaccine therapy, that vaccines

were not applicable in the early stages of acute infections, a divergence of opinion has existed as to the advantages of employing gonococcus vaccine in acute gonorrhea. Much of this opposition to the use of gonococcus vaccine in acute gonorrhea was due to the "fear of the negative phase," with a consequent insufficient dosage to procure any results. That the antigenic or immuno-producing properties of the gonococcus in a surface infection are nil, is evident from the prolonged course such infections run and this is also demonstrated by the fact that complement fixation tests do not show any antibodies or positive reactions from these surface infections. On the contrary, it has been abundantly demonstrated that killed organism injections rapidly train or develop tissue cells for antibody production in the presence of acute infection, and clinical results in the treatment of acute gonorrhea with gonococcus vaccines when given in sufficiently large dosage at proper intervals shows that the gonococcus is no exception to this rule.

In the treatment of gonorrhea it is the end results that count. There is nothing more discouraging than a case of gonorrheal infection which refuses to clear up and such a condition is always due to deep-seated infections which have gone beyond the reach of local treatment and have become too chronic to respond to therapeutic immunization. By giving the vaccine during the acute stages of a gonorrheal infection a systemic immunity is developed which will guard against deep-seated invasions of the gonococcus and by this means will go a long way toward avoiding a chronic infection. That acute gonorrhea is favorably influenced from the hypodermic use of gonococcus vaccine when properly given, is shown by relief from pain at the site of infection and the changed character of the discharge, which usually becomes much thinner and consists mostly of serum, while in many cases the discharge also becomes much less in quantity within a few days after the first inoculation.

The advantages of employing vaccines in conjunction with local treatment were well brought out by N. P. L. Lamb, British Medical Journal, Oct. 6, 1917, in a report of five hundred cases of acute gonorrhea among British soldiers. An analysis of the uncomplicated cases shows that 60 per cent were under treatment 30 days or less, with an average of 19 days. The average duration of all complicated cases was 52 days. That many of these cases were far advanced before treatment was started is shown by the fact that 70 out of the 500 cases had epididymitis and two cases of arthritis developed after the vaccine treatment was started. This indicates that large doses of vaccine in the acute stages of gonorrhea do not produce a negative phase. The most remarkable feature of this entire series of cases is shown in the permanence of the cure, the relapses being less than 1 per cent. The author emphasizes the importance of

this showing and considers it a satisfactory proof of the value of vaccines as a test of cure.

The collective experience among vaccine users in the treatment of acute gonorrhea shows that gonococcus vaccine must be employed in much larger doses than was formerly supposed, to obtain the best results. Instead of giving doses from 5 to 25 million, treatment may be started with 300 or 400 million and the dose rapidly increased to 1,000 million and as much as 2000 million or more gonococci in addition to the other organisms contained in the formula 49. During the acute stages inoculations are made at two to three day intervals. The dose should be increased from the initial dose as rapidly as the tolerance of the patient will permit.

Careful bacteriological investigations show that the staphylococcus soon becomes a complicating factor in gonococcus infections and that as the infection becomes subacute or chronic, the streptococcus, colon bacillus, pneumococcus, pseudo-diphtheria or a combination of these organisms are liable to become associated in the infection. For this reason it has been found practical to employ a mixed vaccine (Formula 49) containing these various organisms, at once, instead of using a straight gonococcus vaccine and waiting until the later stages to use the mixed vaccines, after infections by these organisms have been established. By this means the patient is protected prophylactically toward probable infections.

Since gonorrheal urethritis is essentially a surface infection, the importance of appropriate local treatment to eliminate the germs on the surface of the mucus membrane, really beyond the reach of the immune bodies, should not be neglected. Too often the patient, after finding the discharge almost gone, thinks he is cured and all treatment is neglected, only to find that the trouble will flare up again, whereas if treatment had been continued the entire infection could have been extinguished. While it is important to employ vaccines early it is equally important to continue the treatment for a month or more at weekly intervals, in full size doses, to maintain the immunity that has been attained and by this means completely eliminate possible foci of infection.

The great prevalence of chronic gonorrhea is a reproach on the prevailing methods of treating the acute stages; but since this condition prevails, these chronic cases must be taken care of. That bacterial vaccines are a valuable adjunct in the treatment of chronic gonorrheal infections is now almost universally admitted. Mixed infections in these chronic cases are the rule. The most important of these in addition to the gonococcus are the staphylococcus, colon bacillus, streptococcus, pneumococcus and pseudodiphtheria bacillus. So, to meet this condition, it is necessary to employ a vaccine containing these several organisms (Formula 49). It is important in treating these chronic cases to be

careful and not give too large doses when starting treatment, because unpleasant reactions are more liable to occur from overdosing than in the acute cases and inoculations should be made at somewhat longer intervals. Treatment should be started by giving 0.3 c.c. and the dose gradually increased to 1 c.c. making inoculations at three to seven-day intervals. In some cases it is necessary to work the dose up to 2.0 or 3.0 c.c. but, when giving these large doses, it is best to make the injection in three or four different parts of the body so the tissues at the site of inoculation will not become overtaxed. Local treatment must be carefully followed out. Enlarged prostates must have the pus pockets evacuated by gentle massage and where possible, local treatment should be applied to the focus of infection. Where bacterial examinations show unusual organisms present, a corresponding stock vaccine or an autogenous vaccine should be employed.

A most important factor in successfully treating chronic gonorrhea, is persistence. In chronic infections the immunizing mechanism is often slow to respond and in gonorrheal infections an immunity once established is liable to soon wear off unless the vaccine inoculations are continued. In many cases the immunity builds up slowly where crowding the treatment will not be tolerated. Many cases will require treatment for a year or more before the infection is entirely overcome and it is always wise to continue the injections at one or two week intervals for several months after all symptoms of the disease have subsided to insure permanency of results.

Epididymitis and Orchitis

THE opinion as expressed in current medical literature by vaccine users is practically unanimous in favor of employing gonococcus vaccine in the treatment of epididymitis and orchitis. Early treatment is very important to obtain the best results. Intense prolonged inflammation with pus formation has a tendency to destroy the function of the epididymis. Vaccines can not restore destroyed tissues. With the early administration of gonococcus vaccine the inflammation will be held sufficiently in check to avoid destructive inflammatory developments and instead of leaving the patient with an indurated epididymis the organ is again restored to its former condition.

These acute cases, especially in the presence of fever, tolerate large doses of vaccine at short intervals and it is by giving sufficient dosage repeated at daily intervals that the most striking results are obtained. The initial dose may be 500,000,000 killed gonococci or 0.5 c.c. of Formula 25. The dose may be rapidly worked up to 1.0 c.c. or more, depending entirely on the amount of reaction which develops at the site of inoculation. Injections should be made at daily intervals until the

acute symptoms subside, then three or four days apart until recovery is complete. Many doctors prefer a gonococcus combined vaccine (Formula 49) on the ground that by this means mixed infections, if not already present, will be avoided. There is no good reason why this mixed gonococcus vaccine should not serve every purpose. Clinical observations would certainly justify a trial with Formula 49 in place of 25.

Gonorrhea in Women

IN women, gonorrheal infections are usually extensively mixed even during the early stages of the disease. For this reason a mixed vaccine (Formula 49) should be employed. The principle of therapeutic immunization applies here the same as in men, consequently the same dosage and intervals between inoculations are resorted to. Since the anatomical conditions are different, local treatment and operative interference where necessary, must conform to the natural requirements.

In this connection special mention should be made of the advantages of employing bacterial vaccines in cases where the infection involves the Fallopian tubes. Here the inflammatory process generally seals up the opening with pus accumulation in the tube. Operative interference in the early acute stages is now generally regarded as not advisable on account of the dangers involved and because many of these cases recover spontaneously and thereby save important organs that would otherwise be sacrificed. It is found that in four or six months the pus in these tubes usually becomes sterile when operative methods may be employed without much danger. Here is where vaccine treatment right from the early stages of the infection is very important. By raising the immuno resistance the infection can be kept within bounds and destructive activities prevented. By keeping the infection down drainage through the Fallopian tubes may be maintained and the function of the organ saved. The infection does not subside rapidly but by continuing the treatment persistently month after month good results will follow. The mistake is often made that because this is primarily due to gonococcus infection, a straight gonococcus vaccine will suffice. Mixed infections are the rule, and consequently a mixed vaccine must be employed to obtain the best results. (Formula 49 is the preparation usually employed.)

Gonorrheal Rheumatism

GONORRHEAL rheumatism often presents symptoms so closely allied to other forms of acute and chronic rheumatic arthritis that it is often difficult to make a diagnosis. It is not an uncommon experience to have some one contract gonorrhea who has been subject to rheumatic affections. In such cases the question naturally arises whether the

rheumatism is a recurrence of the old trouble, whether it is due to gonorrheal infection, or possibly to a gonorrheal infection added to a rheumatic infection caused by other organisms. Where a history of gonorrhea exists it is always well to consider the case gonorrheal until it has been demonstrated that the joint infection is not due to the gonococcus.

Gonorrheal rheumatism is in most cases associated with a focal infection in the prostate, Fallopian tubes or other parts where mixed infections with staphylococci, streptococci, colon bacilli, pneumococci, in addition to the gonorrheal infection are common. As common experience shows, focal infections, containing pyogenic organisms, are liable to produce rheumatic joint involvement. In view of the fact that gonococci and other pyogenic organisms preferably grow side by side, in these focal infections, there is every reason to believe that gonorrheal joint involvements are gonococcus. So, in treating gonorrheal rheumatism, the question of mixed infections must always be taken into account and for this reason a mixed vaccine containing gonococci, streptococci, pneumococci, staphylococci, and colon bacilli, or a gonococcus vaccine alternated with a mixed vaccine containing the other organisms, gives the best and most permanent result.

In cases of chronic arthritis the question whether it is of gonorrheal origin may often be settled by giving a large initial dose, 500,000,000 or 1,000,000,000 of gonococcus vaccine. If the infected joints get markedly worse within twelve to eighteen hours with a slight rise of temperature it is safe to conclude that the gonococcus is at least a factor in the arthritis. The fever and joint reaction will subside within a day or two, often with improvement of the joints.

When gonorrheal arthritis develops during the acute or subacute stages of a gonorrheal infection, the question of mixed infections is not of such great importance as far as the joints are concerned, but the focal infection is so complicated with staphylococci involvement that to aid in overcoming this infection staphylococcus at least should be added to the gonococcus vaccine to be employed for acute gonorrheal arthritis.

It is now generally admitted that vaccines are the best therapeutic agents at our command in the treatment of this intractable disease, but while employing the vaccine local treatment at the focus of infection should not be neglected. Strictures should be taken care of, a pus-loaded prostate should be gently massaged and when possible the focus of infection should receive proper local or surgical treatment. To procure permanent relief, it is important that vaccine treatment should be continued in conjunction with other methods until the focus from which the germs were liberated to reach the joints is eliminated.

Later experience shows that where gonococcus vaccine was first used

entirely too small doses were employed. A mixed vaccine containing the organisms usually found in the focal infection associated with gonorrheal rheumatism, Formula 49, is preferably employed. Treatment should be started by giving 0.2 or 0.3 c.c. subcutaneously and gradually increasing the dose to 1 c.c. or more, making inoculations at 4 to 7 day intervals. Where not much reaction follows an injection, the dose may be increased to 1 c.c. within four or five treatments. Usually the dose need not be increased beyond 1.0 c.c. but some cases will require larger doses, possibly 2.0 c.c. or more and the treatment should be continued for several months after all signs of rheumatism have disappeared to obtain a permanent result.

As a rule, improvement will be observed soon after vaccine treatment is instituted and this is particularly so where the case is not of too long standing. In some cases the results are most striking, the entire inflammation subsiding after one or two inoculations, but in such instances vaccine treatment should not be discontinued for at least two months because otherwise they are liable to relapse.

In the old chronic cases where the results are not so good there is good reason to assume that a mixed infection exists, including the same conditions that prevail in deforming arthritis, and consequently must be treated over a long period of time with a vaccine that contains the gonococcus in addition to the combined vaccine employed in rheumatoid arthritis.

GUMBOILS[1]

GYNECOLOGICAL INFECTIONS

ASIDE from gonorrheal infections, there are many cases of suppressed pelvic infections—metritis, endo-metritis, vaginitis, salpingitis, ovaritis—due to colon bacillus, streptococcus, pneumococcus and staphylococcus infections. Here a course of vaccine treatment with Formula 35 in conjunction with local treatment will give results that cannot be attained with local treatment alone. Many obscure symptoms of nervousness, nausea, neuritis, etc., disappear after using the vaccine. Leukorrhea, which is such a disagreeable ailment with many women, will disappear under this treatment. In these chronic conditions, treatment is started with the usual dose 0.2 or 0.3 c.c. and the dose gradually increased to 1 c.c. inoculations being made at 5 to 7 day intervals. In obstinate cases, treatment must be continued for six months or more.

In acute pelvic cellulitis, the same vaccine is employed, but being an acute toxic infection, 1 c.c. doses should be given and repeated at daily intervals until the acute symptoms subside and at 3 to 5 day intervals during convalescence. Most excellent results are obtained by this

[1] See Mouth Infections.

method. If given early, the infection can be aborted and thus prevent abscess formation.

Thrombo-phlebitis is a condition that usually develops from an infection of thrombi in the veins beneath the placental site, or from the pelvic veins which extend from thence to the larger veins. This may readily produce an extensive thrombosis. The same bacteria which are responsible for other gynecological infections are also responsible for infections of these veins. Often small blood clots in the infected veins soften and the broken-down substances enter the blood stream, setting up a pyemia or septicemia. This condition usually sets in during the second week of the puerperium, the infection which is of a mild character, gradually extending along the veins. This shows the importance of therapeutic immunization, even in mild infections during the puerperal state. If such infections were aborted during the early stages, thrombo-phlebitis would be avoided. Where extensive thrombi develop, the condition is always serious. Here we have a blood infection combined with the plugging of large veins which interferes with the circulation of the leg, favoring the formation of metastasis.

Being an extremely acute infection, vaccine treatment should be started at once by giving 1 c.c. doses of Formula 35 at daily intervals and in extremely bad cases twice daily. After the fever subsides, the intervals are extended to 2 or 3 days and continued during convalescence. The results are uniformly good. If the vaccine is used early, the infection can be aborted with a resulting rapid recovery. Even far advanced cases should not be abandoned. Apparently hopeless cases have been saved by induced immunization with this vaccine.

Puerperal Sepsis

FEVER a few days after a confinement is always regarded with apprehension, because it may be the first indication of the development of a dangerous infection. While it is true that we often have in these cases a rise of temperature which subsides spontaneously in a few days, it is just this hope that nothing serious will happen that is responsible for costly delay in instituting therapeutic immunization. The best authorities consider a temperature of 100.4° F. inside of ten days after a confinement with few exceptions, as being due to infection and that in slight infections the fever rarely goes beyond 101°. When the temperature reaches 103° or 104° inside of 3 or 4 days, the infection must be regarded as belonging to the severe types. When associated with rigors, it is probable that a blood infection has taken place.

Local treatment, with the object of destroying the infection, is at best difficult to carry out because the entire surface of the uterine cavity cannot be reached. Curetting, unless very carefully done, will do more

harm than good by exposing new surfaces for infection and by manipulating an inflamed organ. If the infection has extended into the uterine tissue, it can not be reached by any local treatment.

In puerperal sepsis, the streptococcus is by all odds the most dangerous micro-organism to deal with. The colon bacillus, pneumococcus and staphylococcus are also frequently present, either as primary invaders or as complicating factors in a mixed infection. Where there is a gonorrheal infection, the gonococcus is also found. Other organisms of less pathogenic significance may also be present.

Vaccine treatment should not be delayed for the purpose of making a bacterial examination. Early immunization is of more importance in these cases than an exact diagnosis. A streptococcus-colon bacillus combined vaccine (Formula 35) serves the best purpose. Treatment should be started with 1 c.c. and injections made at daily intervals until the fever and other toxic symptoms subside. When treatment is started early, we may confidently expect a normal temperature within one or two days. In these cases, it is a mistake to discontinue vaccine injections after the temperature comes down because they are so liable to relapse. It is better to continue the vaccine for two days after a normal temperature at daily intervals and then extend the interval to 2 to 4 days. It is also of advantage to give the vaccine at weekly intervals for several weeks after convalescence.

Blood cultures to determine whether a blood infection has developed should be made as soon as possible. The blood is drawn from a vein with a sterile hypodermic syringe and mixed with liquid culture media in a sterile flask and incubated. Making bacterial examinations of the uterine contents is unsatisfactory. If an unusual organism should be found in the blood, a corresponding stock or autogenous vaccine may be prepared and given.

In case there is gonorrhea present, a gonococcus vaccine should be given in conjunction with the other vaccine.

HAY FEVER

HAY FEVER is primarily a pollen irritation in persons sensitized to certain pollens. By means of skin tests, we are enabled to determine the particular pollen a hay fever sufferer is sensitized to. From extensive application of these tests in hay fever cases, it has been shown that hay fever patients are usually sensitized to several pollens—and skin tests also show pollen sensitization in persons who do not show symptoms of hay fever when exposed to the same pollen.

Invasion by pathogenic bacteria—streptococci, pneumococci, staphylococci, etc.—of the pollen irritated respiratory tract is a constant feature of hay fever and in fact soon becomes the most important factor of

the ailment. The febrile symptoms are in all probability entirely due to this bacterial invasion. It is for this reason that by far the best results in the treatment of hay fever have been obtained from the use of bacterial vaccines. In some cases it appears that better results are obtained by giving pollen vaccine in conjunction with bacterial vaccines. So when treating hay fever it is best to always immunize the patient to the common pathogenic organisms responsible for respiratory infections. A polyvalent combined vaccine (Formula 40, 36 or 38) is the formula usually required. In ordinary cases Formula 40 serves the best purpose. If the case is complicated by the Friedlander bacillus, Formula 36 should be employed and, if the influenza bacillus is present, Formula 38 would be the proper combination.

Dosage should be gauged by the amount of reaction at the point of injection. The dose should not be so large that constitutional reactions are produced. A red infiltration two or three inches across at site of injection is all that is required. The initial dose should not exceed 0.5 c.c. or 8 minims. If not much reaction follows, the dose may be rapidly increased to 1 c.c. Inoculations should be made at about 3 day intervals. In many cases the hay fever symptoms subside entirely after three or four inoculations but the treatment should be continued for several weeks at 4 to 6 day intervals to guard against a relapse. In other cases the disease runs a decidedly modified course. If the case does not clear up entirely, treatment should be continued and in some cases it is advisable to give the vaccine at 2 day intervals. The vaccine should be injected into the connective tissues under the skin and a new area should be selected each time.

The severe symptoms of hay fever may also be prevented by immunizing the patient to respiratory infections by giving 4 or 5 doses at 5 day intervals prior to the usual onset of symptoms. In many cases only slight symptoms develop which will subside entirely after a few more injections. If severe symptoms should develop, treatment must be continued the same as if no vaccine had been employed prior to the attack.

Occasionally hay fever becomes complicated by an unusual organism. If a case should not improve promptly under the vaccine treatment, a bacterial examination might determine the presence of an unusual organism when an autogenous or corresponding vaccine should be employed.

HORDEOLUM[1]

HEART INFECTIONS

HEART infections—endocarditis, pericarditis and myocarditis—are sufficiently common and because of their seriousness, assume a prominent position in everyday practice. Heart infections are probably

[1] See Eye Infections.

always preceded by a blood infection. Streptococci are most frequently responsible for endocarditis, but pneumococci, staphylococci, gonococci and other organisms are also occasionally found. What is true of endocarditis also holds good with myocarditis and pericarditis.

When considering vaccine treatment in heart infections, it must be remembered that by curing an infection, tissues that have been destroyed during the course of an infection can not be restored. A heart valve that has been crippled by germ activities can not be made to function properly after the infection has been eliminated. For this reason early treatment is most important, not when heart lesions are detected but before this, during the presence of the blood infection, before heart infection develops. By this means the infection can be eliminated before the heart becomes involved. Good results are also obtained when vaccine treatment is started during the early stages of heart involvement, before active destructive processes have taken place. By inducing early immunization, the inflammation in the heart valves will subside and leave them in a condition so they are able to function properly.

Heart infection is a common complication of acute rheumatic arthritis and is the primary cause of death from this disease. This alone should be sufficient reason for giving bacterial vaccines in the treatment of rheumatic fever because it is found that by treating these cases with vaccines heart infections are avoided, providing the treatment is started before heart complications have developed. The same may be said of tonsillitis and sinus infections which are so often followed by heart infections.

A mixed vaccine containing streptococci, pneumococci, and staphylococci (Formula 6) is preferably employed. In the acute febrile conditions, 1 c.c. doses are given at 1 to 2 day intervals. After the acute symptoms subside, injections are made at 4 to 6 day intervals. In chronic cases, the injections are made in accord with the rules which apply to other chronic infections, i. e., start treatment with 0.2 c.c. of the combined vaccine and repeat inoculations at 4 to 6 days, increasing the dose at each injection 0.1 to 0.2 c.c. depending upon the amount of local reaction.

IMPETIGO[1]

IMPETIGO is a skin infection due to the staphylococcus and sometimes complicated with the streptococcus. In the former a staphylococcus vaccine (Formula 22) and in the latter condition, a strepto-staphylo combined vaccine (Formula 10) is employed. The condition is rather acute and requires inoculations at 2 to 3 day intervals, starting with 0.3 c.c. and gradually working the dose up to 1 c.c.

1 See Dermatitis also.

INDIGESTION[1]

INFLUENZA[2]

IT HAS been quite evident that epidemic influenza is caused by an infecting organism that lowers the resistance of the infected person to pneumococci, streptococci, staphylococci, influenza bacilli and other organisms commonly responsible for infections of the respiratory organs. This conforms to the common experience that the real danger in epidemic influenza is due to pneumonia or broncho-pneumonia caused by pneumococcus, streptococcus, influenza bacillus, and staphylococcus infections. This knowledge makes the use of a combined vaccine containing these various organisms (Formula 38) a logical procedure both as a preventive and curative measure in influenza.

Our experience with Formula 38 during the influenza epidemic of 1918 and since then has been very extensive which makes logical deductions possible. In the presence of an epidemic our experience shows that preventive inoculations are entirely practical. While these inoculations do not entirely prevent attacks of influenza, it is entirely within ascertained demonstrations that those who received three or more doses of Formula 38 were much less liable to contract the disease and those who did contract it had much milder attacks, making deaths among those receiving the inoculations so few that the mortality rate dropped to less than one in three thousand of those receiving the inoculations, and, as far as we have been able to ascertain, no one died who received the vaccine prophylactically and therapeutically if he contracted the disease. In the presence of an epidemic, preventive inoculations are best made at 2 or 3 day intervals, the first injection being 0.5 c.c., the second 0.8 c.c. and the third 1 c.c. To be on the safe side, it is well to give two or three more injections of 1 c.c. at weekly intervals. In case there is no immediate danger of an epidemic, inoculations may be made at 5 to 7 day intervals.

In the treatment of influenza, the dosage and intervals between inoculations depend largely on the severity of the case—the more severe the case the larger the dose and the shorter the intervals between the inoculations. In the ordinary cases without lung complications, treatment is started with 0.5 c.c. and inoculations are made at 3 day intervals, gradually increasing the dose to 1 c.c. After the acute symptoms subside, inoculations are made at 3 to 5 day intervals. In the more severe cases with high temperature, 1 c.c. doses are given at daily intervals until the acute symptoms subside and at 3 to 5 day intervals after that until convalescence is complete. If indications of pneumonia development are present, 1 c.c. doses are given at twelve hour intervals until the

[1]See Gastro-Intestinal Infections.
[2]See Rhinitis and Pneumonia.

temperature comes to normal when the intervals may be extended to one or two days, depending on the progress of the case. During convalescence vaccines are given at about 5 day intervals. In bad pneumonia cases, the dose may be worked up to 1.5 or 2 c.c. given at 8 to 12 hour intervals, changing the site of inoculation at each injection. When giving large doses, the vaccine should be injected in two or three different parts of the body. Many bad cases of influenza start with a subnormal temperature and great prostration. These cases are particularly dangerous, and it is found that by giving the vaccine promptly there will be a rise in temperature associated with a general recuperation. Influenza pneumonia cases are treated essentially the same as other pneumonias. See pneumonia.

IRITIS[1]

ISCHIO RECTAL ABSCESS[2]

JAUNDICE[3]

KERATITIS[1]

LARYNGITIS[4]

LARYNGITIS is due to the same infecting organisms which cause bronchitis and from an immunologic standpoint should be treated the same.

LEUKORRHEA[5]

LOBAR PNEUMONIA[6]

MASTITIS

MASTITIS is due to an infection of the milk ducts of the mammary gland. The common pyogenic organisms, of which the staphylococci are the most important, are usually the responsible invaders. An inflammatory condition of the gland is sufficient evidence that an infection has developed and calls for immediate vaccine treatment. A mixed vaccine containing the usual infecting organisms (Formula 6 or 35) is employed to advantage. The size of the initial dose is gauged by the amount of infection present when treatment is started. In the minor cases from 0.2 to 0.3 c.c. should be given as the initial dose. In cases with extensive involvement with fever the initial dose should be from 0.5 to 1 c.c. Inoculations should be made at 1 to 2 day intervals until the acute symptoms have subsided and then at 3 to 5 day intervals. If treatment is started early, the infection can be aborted without abscess formation. In cases where an abscess is present, drainage must be established, but meantime the vaccine should be employed to hasten recovery.

[1]See Eye Infections.
[2]See Abscesses
[3]See Cholecystitis.
[4]See Tuberculosis also.
[5]See Gynecological Infections.
[6]See Pneumonia.

MASTOIDITIS[1]

METRITIS[2]

MOUTH INFECTIONS

INFECTIONS of the mouth are common and cause much pain and often permanent trouble. Slight superficial ulcers of the mouth or aphthæ are the result of superficial infections by the usual infecting organisms found in nose and throat infections—streptococci, pneumococci and staphylococci. When acute infections of the throat exist, very slight injury to the mucous membrane of the mouth will suffice to start one of these ulcers and from the frequency that this condition is met with during acute colds it appears that these localized infections can take place without a previous abrasion of the mucous membrane.

In adults these mouth ulcers usually heal spontaneously especially when local treatment of an antiseptic nature is applied, but in infants we have seen cases where practically the entire mouth was involved. The use of bacterial vaccines is of distinct advantage in all these cases. It will be found that the ulcers will heal much more rapidly and the tendency for new ulcers to develop will be avoided. Some people are subject to thrush and while the ulcers usually heal rapidly, new ones appear at short intervals. In these cases, vaccines are also of great value in that approximately permanent results may be obtained.

Among the acute infections of the mouth, abscess formation at the root of teeth, known as septic apical and mandibular abscesses, are the most troublesome to handle and often lead to the loss of teeth that can be saved by the timely use of bacterial vaccines and at the same time relieve much pain. An acute abscess at the root of a tooth is a small affair which, by early immunization can be aborted, with subsequent absorption of the small amount of pus present. In many instances, immunization in this manner will be instrumental in saving the tooth. Necessarily, the earlier in the course of abscess formation immunization is established the better are the chances to avoid permanent injury to the tooth and make its removal unnecessary. The early symptoms of apical abscess formation are deep-seated pain in the tooth with a feeling that the tooth is too long and very painful when biting. As the infection develops, much swelling of the gum and surrounding tissue, with contiguous lymphatic gland involvement, takes place.

Streptococci, pneumococci and staphylococci are, with few possible exceptions, the responsible infecting agents and would require a vaccine containing these organisms (Formula 6). It being an acute affair, vaccine injections should be made at 1 to 2 day intervals. The initial dose should

[1]See Ear Infections.
[2]See Gynecological Infections and Gonorrhea

conform to the amount of inflammation present, ranging from 0.5 c.c. to 1 c.c. After the acute symptoms subside, inoculations should be extended to 4 to 6 day intervals. This treatment is of inestimable value in these cases. As a rule, relief from pain will follow within twenty-four hours and meantime the swelling will also begin to subside.

Gumboils should be lanced and where fistulous openings exist, necrotic bone should be looked for and removed. Bacterial vaccines should be given to hasten repair.

MYELITIS[1]

NASAL INFECTIONS[2]

NEPHRITIS

THE bacteriology of the urine in health and disease has been extensively studied. To arrive at a positive conclusion whether or not the urine is sterile in health is surrounded with some difficulty because staphylococci are frequently present in the urethra. So, even when a specimen is collected by catheterization, there is always a chance of urethral contamination, but the number of organisms from such a source are always small, and when a considerable number of germs are found in the urine it is safe to assume that the organisms are present in the urine.

Some extensive work on the bacteriology of urine was done by Drs. George F. and Gladys R. Dick (Journal A. M. A., July 3, 1915, p. 6), who, to avoid contamination, collected the urine by catheterizing the ureters. Cultures of 2 c.c. of catheterized urine were made in deep tubes of dextrose agar; aërobic and anaërobic cultures on blood ascites agar were made from the sediment of 15 c.c. of centrifuged urine.

A study of their work shows that the urine in health is for all practical purposes sterile, that the streptococcus is the most common known pathogenic organism found in both the acute and chronic cases of nephritis. They also found that in cases of coccus infections, organisms identical to those present in the infected focus may also be found in the urine without the presence of albumin, casts or other indications of kidney disease. This is in accord with the findings of other investigators and would indicate that the kidney is capable of eliminating live pathogenic organisms from the blood as it passes through the kidney.

The frequency with which streptococci are found in the urine in scarlet fever, pneumococci in pneumonia, and micro organisms in typhoid, and other acute infections without albuminuria or other indications of kidney involvement is good evidence that germs may pass through the kidney without injuring it. The frequency with which nephritis follows scarlet fever shows, however, that streptococci may become active pathogenic agents in kidney inflammations.

[1]See Osteomyelitis
[2]See Rhinitis.

Two concepts prevail concerning the cause of kidney inflammation; A, that toxic materials passing through the kidney while being eliminated irritate the kidney structure and lead to inflammation; B, that kidney inflammation is due to a direct infection of the kidney substance. That irritating substances eliminated by the kidneys do cause kidney inflammation is well illustrated in cases of bi-chloride of mercury poisoning, etc., but we find that these cases recover rapidly if the specific poison is disposed of. In case a nephritis develops during the course of an acute infection, it is believed by some that the kidney inflammation is similarly due to the elimination of toxic materials, but this contention does not appear well grounded because in the vast majority of acute toxic infections no evidence of kidney inflammation develops. From our present knowledge of inflammatory processes we must conclude that an active nephritis, except when due to some specific poison, must be regarded as due to infection. [See Editorial J. A. M. A., Dec. 15 1923, p. 2035]

The fact that so many cases of nephritis date back to the various acute infections is strong evidence that the kidney infection is a sequence to such an infection. It is not uncommon to have cases of nephritis follow tonsillitis or a "cold," and in such cases we must conclude that the infecting organisms responsible for the primary infection developed a metastasis in the kidney. This would emphasize the importance of therapeutic immunization with vaccines in the treatment of colds and other minor infections. By this method sufficient immunity is developed during the primary infection to avoid the concurrent or subsequent kidney involvement. At least this is our experience, to our knowledge no case of nephritis has developed in cases where vaccines were employed for the treatment of the primary infection. Since the streptococcus is always a primary infecting agent or a complicating factor in infective processes that lead to the kidney infection, and since careful bacterial examinations of the urine in cases of nephritis uniformly show the presence of streptococci, it is necessary to regard all cases of nephritis as being fundamentally due to streptococcus infection. Other organisms are also frequently found in the urine of nephritic cases, but these may be regarded as secondary invaders. So, in the selection of a vaccine for the treatment of nephritis, it is essential that the streptococcus should be an important constituent, and that the other organisms usually found as secondary invaders should also be contained in the vaccine. The combination most generally employed contains streptococci, pneumococci, staphylococci and colon bacilli (Formula 35).

In the treatment of nephritis a clear distinction must be made between extensive acute and chronic varieties. In acute nephritis the inflammation of the kidney is often so intense that the entire function of the organ is suspended. This makes the infection a very serious one, not so much

from the amount of tissue involved and the amount of toxic materials produced from the infected tissue, as from the fact that a most important organ of the body has been deprived of its ability to function. In case of erysipelas, for example, the streptococcus will involve much more tissue than in a case of nephritis, but in this instance, the tissues involved are not essential toward sustaining life while the infection is running its course as is the case in nephritis. This makes it doubly important in the case of kidney infection to get rid of the inflammation as soon as possible, before enough of the waste products which the kidneys otherwise eliminate, have time to accumulate in the body to cause death by uremic poisoning. The earlier in the course of the disease, immunity can be established, the better are the chances for recovery. This necessitates the administration of a proper combined stock vaccine at once, preferably Formula 35. To delay vaccine treatment in such a case until a careful bacterial examination of the urine can be made to determine the infecting organism might be responsible for a fatal termination. The infection being acute, probably associated with considerable fever, a large dose 1.0 c.c. repeated at daily intervals for two to four injections is indicated, then at 2 to 4 day intervals if the patient progresses favorably. It is very important that the vaccine should be employed early, before extensive uremic poisoning has set in, because tissues are much more responsive to the stimulating influence of the vaccines for antibody formation before the vitality of the patient has become exhausted. Meantime, elimination by catharsis, hot packs, drug-induced perspiration should be persistently carried out to sustain the life of the patient until immunity with a resulting elimination of the kidney inflammation, becomes established.

In the less acute cases where the kidneys continue to function fairly well, these adjunct measures to vaccine treatment are not so important. As a rule, they progress favorably under the vaccine treatment. In this class of cases, treatment should be started by giving 0.2 c.c. and gradually increasing the dose to 1.0 c.c., making inoculations at 3 to 5 day intervals, depending on the reactions and progress of the patient. Cases of nephritis of pregnancy that are not too far advanced would come under this class.

Chronic cases of nephritis progress under the vaccine treatment in direct proportion to the permanent damage that the kidneys have sustained before therapeutic immunization is instituted. Kidneys that have become contracted as a result of long-continued inflammation cannot be expected to be restored to function normally. If, however, sufficient kidney structure remains which can function normally after the infection has been abated, to eliminate the waste products of body metabolism, health can be restored. It is impossible to know in advance just how much of the kidney function can be restored to health. For this reason,

no case of nephritis should be abandoned until the vaccine method has been given a thorough trial.

In the treatment of chronic nephritis, the same streptococcus, pneumococcus, staphylococcus, colon bacillus, combined vaccine (Formula 35) is employed that is used in the acute cases. The dosage and management of the case, however, is different. Following the rule of treating chronic conditions, treatment is started with the usual dose, 0.2 c.c. and administered at long intervals 4 to 7 days apart. The dose is gradually increased to 1.0 c.c. or more, but should not be increased so rapidly that marked reactions follow the injection. Treatment should be continued until the urine clears up or until it is evident that the damage cannot be repaired. Treatment should be continued for at least six months before considering the case beyond improvement.

The statements made naturally presuppose proper and timely surgical interference where indicated. This applies to vaccine therapy in general.

NEURITIS

IT is striking that so many doctors disregard the use of vaccines in the treatment of the various forms of neuritis. Conventional remedies certainly are inefficient, and for this reason alone it would appear that every doctor would at once avail himself of this remedy, because it does not only give relief, but actually effects cures.

That neuritis is due to infection is now well established. Neuritis frequently follows such acute infections as scarlet fever or septicemia, or, like rheumatism, it may develop after an attack of tonsillitis, or some infective process of the mouth, teeth, nose, throat, sinuses, middle ear or bronchi.

We now know that the streptococcus, pneumococcus and even the staphylococcus often gain entrance to the blood current from these localized ailments, and through the blood these germs are carried to distant parts of the body, where localized infective processes develop. This is what evidently takes place in rheumatism, endocarditis and osteomyelitis.

In rheumatism the synovial membrane and connective tissues around the joints are attacked, and the infection, while often very acute, does not go on to suppuration. In the subacute and chronic types the infection continues for a long time in the connective tissue around the joints without material change in the character of the inflammation. This class of subacute and chronic infections of connective tissues is particularly liable to take place from streptococcus infections.

Rosenow, Journal A. M. A., Nov., 1915, experimentally produced neuritis in lower animals by intravenous injections of streptococci isolated from focal infections of cases suffering with neuritis. The fact that

streptococci and certain types of pneumococci readily invade connective tissues with a tendency to produce subacute or chronic inflammatory processes, would lead us to believe that in neuritis the connective tissue connecting the nerve fibres instead of the nerve structure itself, is involved. This would account for the pain and irritated condition of the nerve, whereas if the nerve structure itself were involved in the infection, the function of the nerve would probably be destroyed. Long continued infection of connective tissues produces a characteristic proliferation and hardening; just the condition found in chronic sciatica or sciatic neuritis where the nerve is found indurated and enlarged.

The infectious character of neuritis being recognized, vaccine treatment suggests itself as a logical procedure. From the character of the infection, it would appear that a streptococcus or pneumococcus vaccine should be employed, but from extensive experience we find that a combined streptococcus, pneumococcus, staphylococcus, colon bacillus vaccine (Formula 35) gives the most consistent results. In many cases, however, where the neuritis is associated with bronchitis, sinus or throat infections, Formulas 40, 38, or 36 may be employed to advantage.

As far as the application of vaccines is concerned, it makes little difference whether the neuritis assumes the form of sciatica, tic-douloureux or multiple neuritis. The results obtained from vaccine injections are in direct proportion to the length of time the neuritis has existed before vaccine treatment is started. In cases of but few weeks' standing, distinct benefit will be observed after the first or second injection, whereas, chronic cases will respond more slowly, probably requiring one or two months' treatment before much improvement is observed. This closely follows our experience with other infections; the more chronic the infection the longer treatment must be continued to effect a cure. In cases of several years' standing, it is often necessary to continue treatment for six months or a year before desired results are obtained.

In the application of the vaccine, the same rules should be observed that are employed in other forms of chronic infections. Treatment should be started with 0.2 c.c. of the usual stock suspension, and the dose gradually increased to 1.0 c.c. or more, making inoculations at 5 to 7 day intervals. Marked reactions should be avoided. This is best done by gauging the dose to the amount of reaction produced by the previous injection. If the previous injection caused considerable reaction, the subsequent dose should not be materially enlarged. It is also important that the vaccine should not be injected in the same part of the body a large number of times. The tissues where a number of injections have been made develop a tolerance to the vaccine and become less responsive to antibody production than new tissue. So, when giving the vaccine a new area for the injection is preferably employed with each treatment.

Too large dosage and giving the vaccine at short intervals as a rule will not hasten recovery. Chronic infections will not tolerate crowding in vaccine therapy, but by persistent treatment, over a long period of time, with careful observation of reactions and dosage adjusted thereto, good results may be confidently expected. The results from the use of vaccines in the treatment of neuritis have been so striking that no case should be considered hopeless.

OPTHALMIA, SYMPATHETIC

IT is quite probable that the involvement of the healthy eye is due to spreading of the infection from the diseased one along the sheath of the optic nerve. The vital necessity of saving the sight calls imperatively for the injection of vaccines for the purpose of arousing general immunization and thereby limiting the process. There can be no harm, and there may be priceless gain, to the patient, from injections of Formula 6.

ORCHITIS[1]

OSTEOMYELITIS, OSTEITIS AND PERIOSTITIS

ONE striking characteristic of bone and joint infections is that the same micro-organisms that cause infections of the soft tissues of the body are also responsible, with few exceptions, for infections of the bony structures, and in the treatment of bone infections with vaccines it is well to keep this in mind. In the early acute stages, before surgical intervention is advisable, much can be accomplished by giving vaccines empirically on a clinical diagnosis. In making a diagnosis for the purpose of selecting a vaccine, a possible tubercle, gonorrheal or syphilitic infection should always be carefully considered, and when present, corresponding specific treatment should be instituted. When a localized inflammatory focus on some bone has persisted after an attack of typhoid fever, a possible typhoid infection should be suspected.

The most common infecting organisms of joints and bones are streptococci, staphylococci, pneumococci and colon bacilli. More rarely we have Friedlander bacilli, pyocyaneus, and diphtheroid bacilli. One characteristic symptom of acute joint and bone infections is severe pain; and as a rule, when severe acute pain comes on suddenly, it may safely be considered to be due to pyogenic organisms, and the immediate administration of a combined vaccine containing at least streptococci, staphylococci, and pneumococci is indicated. Early immunization is the most essential factor in the successful treatment of these cases. If given sufficiently early, before pus formation has taken place, the vaccine will as a rule stimulate enough anti-body production to prevent

[1]See Gonorrhea.

suppuration and often will avoid the necessity of an operation. If an operation for the evacuation of pus should become necessary, it will be found that the immunizing influence of the vaccine will promote healing with a much more rapid recovery than where no vaccine has been administered. Where operative interference becomes necessary for the purpose of establishing drainage, cultures should always be taken for the purpose of making a bacterial examination and if necessary an autogenous vaccine can then be prepared.

The organisms responsible for osteomyelitis are the staphylococcus, the streptococcus, the colon bacillus, the typhoid bacillus, the gonococcus and the tubercle bacillus. Of these the staphylococcus aureus is the most common. In the early stages an extensive blood infection often accompanies the bone involvement. On theoretical grounds some writers consider the use of vaccines contraindicated where such an extensive acute infection exists, and contend that if vaccines are employed, exceedingly small doses should be given, but experience shows that such theoretical conceptions are based on a false premise. Many of these cases are very toxic as shown by the temperature, pulse-rate and nervous symptoms. This shows that immunization with adequate antibody formation is retarded or inhibited by the virulence of the invading organism. To depend on the antigenic properties of such devitalizing agents is unscientific and disastrous. Antibody production to stop the ravages of the infecting organism is of utmost importance. As has been pointed out before, live virulent organisms when circulating in the blood do not arouse tissue cell activities as adequately for antibody production as when tissues themselves are involved; and when tissues are attacked by live virulent organisms the devitalizing influence of the germs hinder antibody production, and this applies most emphatically to staphylococci, and streptococci. The result is that usually extensive pus formation and tissue and bone destruction takes place before sufficient antibody production is aroused to overcome the infection. Staphylococcus infections have a distinct tendency, as shown in cases of boils and furunculosis to develop new foci of infection, demonstrating that immunization develops slowly under the influence of the live organisms. This same tendency to develop new foci of infection, with retarded immunization is also observed in cases of osteomyelitis. It has been our experience, and has been abundantly verified by other observers, that the very best results are obtained when vaccines are given as early as possible in acute infections, and this holds good whether the infection involves the blood or is localized. Furthermore, to secure the best results larger doses should be given than when treating less severe or subacute or chronic infections, and the vaccine should be given at daily intervals for two or three days.

Before a positive bacterial diagnosis can be made from pus examination or blood culture the patient should be immunized by giving a polyvalent stock vaccine containing staphylococci, streptococci, pneumococci and colon bacilli, in the full average dose, about twice or three times the usual initial dose, and this repeated at daily intervals for two or three days. Later, when the infection is under control, the interval is lengthened to three to five days.

If bacterial examination should show other organisms present, corresponding vaccines should be employed, and when the infection is due to staphylococcus it may be necessary to work the dose of staphylococcus vaccine up to several thousand million organisms before a cure is effected.

In subacute and chronic cases with fistulous openings a careful search for necrotic bone should not be neglected and when this is found, removed. Staphylococcus infections of the soft tissues near necrotic bone infections have a tendency to heal slowly even after the dead bone has been removed, but it is found that when staphylococcus bacterins are employed this tendency is avoided resulting in a rapid healing of the wound. When no dead bone is present many fistulous openings will heal under the influence of the vaccine and when healing does not take place a tubercle infection is probably a factor. Careful bacterial examinations should be made in all these cases, because old fistulous openings are liable to harbor a large variety of organisms.

OTITIS MEDIA[1]

OZENA[2]

OZENA as a result of extensive bacteriological work was for a time regarded as being due to a special organism but at the present time it is generally believed to be due to some varieties of the Friedlander bacillus. Streptococci, pneumococci and staphylococci are common associates in the infection. The infection is associated with a very disagreeable odor and is very obstinate. In view of the unsatisfactory results from local treatment alone and from the many good results that have been obtained from vaccines, this treatment should be resorted to. Formula 36 contains some strains of the Friedlander bacillus isolated from cases of ozena. Some very good results are being obtained. Treatment is started with the usual dose 0.2 c.c. and gradulaly worked up to 1 c.c. inoculations being made at 4 to 6 day intervals.

[1]See Ear Infections.
[2]See Rhinitis and Colds.

PERITONITIS[1]

PERTUSSIS[2]

PHARYNGITIS[3]

PHLEBITIS, THROMBO-PHLEBITIS

PHLEBITIS is not uncommonly seen before and during confinements, especially in cases of varicose veins, and for this reason this ailment deserves mention here. The staphylococcus or streptococcus are usually the infecting organisms, although other germs may also be present. Streptococcus-staphylococcus mixed vaccine, when used in these cases, gives the best results. We have seen conditions after confinement, which from the extent of the veins involved promised serious trouble, that disappeared after a few injections of streptococcus-staphylococcus vaccine. One case occurred in a woman during the seventh month of gestation. The veins of one leg had for some time been varicosed and at this time became extensively inflamed. She was very much alarmed on account of a very tedious recovery from the same trouble on a previous occasion. She was assured that the vaccine method of treatment would avoid any serious complications and this relieved her mental state. After two inoculations at five-day intervals the entire inflammatory process subsided and she went on to full term without further trouble. The same treatment should be equally applicable in other cases of phlebitis.

In thrombo-phlebitis we have a condition that usually develops from an infection of thrombi in the veins which extend from thence to the larger veins. This may readily produce an extensive thrombosis, Frequently small blood-clots in the pelvic veins soften and the broken-down substances enter the blood stream, setting up a pyemia or septicemia. Staphylococci, streptococci, or, at times, both organisms are found. This condition usually sets in during the second week of the puerperium, the infection, which is often of a mild character, gradually extending along the veins. If such an infection were aborted in this early stage by the use of vaccines, thrombo-phlebitis and its attendant pain and danger would be avoided. Where extensive thrombi develop the condition is always very serious. Here we have a condition of a general infection combined with the plugging of large veins which interferes with the proper circulation of the blood in the leg, favoring the formation of metastasis. From the serious character of the infection a

[1]See Gynecological Infections, Appendicitis, Puerperal Sepsis, and Blood Infections.
[2]See Whooping Cough.
[3]See Rhinitis and Colds

high mortality rate under conventional treatment should be expected. Lea ("Puerperal Infection," p. 178) places the average mortality at 60 per cent.

PNEUMONIA AND ITS COMPLICATIONS

THE most important proposition confronting the medical profession at the present time is the successful treatment of pneumonia. Pneumonia is still responsible for more deaths than any other disease in normal times and in case of influenza epidemics is the real cause, as a complicating factor, of the enormous mortality rate. Under the prevailing or expectant method of treatment the mortality rate runs anywhere from 10 to 40 per cent, depending on the virulence of the prevailing infecting organisms responsible for the pneumonias. Such a high mortality rate conclusively shows that the usual methods of treatment employed are radically inefficient.

Much has been done in classifying the various types of pneumococci that are responsible for pneumonia and a few years ago it was believed that types I, II and III were responsible for practically all fatal cases of pneumonia, but during the influenza epidemics of 1918 and 1920 it was found that pneumococci belonging to the conglomerate group classed as type IV were about as frequently found as the prevailing organisms in fatal cases as types I, II and III.

Most of the leading pathologists failed to recognize the streptococcus as a serious complicating infecting organism until it was shown that a hemolytic streptococcus was usually found as a pathogenic factor in fatal cases of pneumonia in the army camps during January, February and March of 1918, when the mortality rate among the recruits who contracted pneumonia was so high. The importance of the streptococcus as an active infecting agent was again demonstrated in the pneumonias that developed during the influenza epidemic in the fall of 1918 and winter of 1920. In fact the streptococcus factor of the infection was so pronounced during these epidemics that the rapidly fatal cases with lung œdema, followed by cyanosis, were primarily attributed to the ravages of this organism. The bacillus of Pfeiffer or so-called influenza bacillus no doubt also plays an important role as a complicating agent in many cases. In some cases the staphylococcus aureus has been found to be the predominating organism. In cases of broncho-pneumonia all these various organisms may be expected to be present. All these findings are a verification of our contention, held for many years that mixed infections are the important elements that enter into the etiology of pneumonia amd must be reckoned with in the application of immunologic therapy.

On the theory of absolute specificity in applied immunology, much importance has been placed on the necessity of determining the type of

pneumococcus which is responsible for the infection before instituting immunologic treatment. That immunities which develop from vaccine injections are specific is established, but this applies most particularly to immunizing responses from the various types in certain groups.

The theoretical contention that vaccines are contraindicated in extensive acute infections has been mainly responsible for the vaccine treatment of pneumonia not coming into general use long before this and curious as it may seem, those who are opposed to the use of vaccines in pneumonia, have had no experience with them in the early treatment of the disease. In order to clear up the fallaciousness of this theoretic opposition to the use of vaccines in the treatment of pneumonia, it will be necessary to elucidate some of the fundamental activities of the immunizing mechanism.

When infecting organisms gain entrance to the tissues or fluids of the living body, they maintain themselves by the ferments which they secrete by means of which they prepare the food on which they live, grow and multiply. In pneumonia, for example, the pneumococcus gains entrance to the blood stream from a primary localized infection of some portion of the respiratory tract. From these primary localized surface infections, pneumococci, by a process of growth, work their way through the walls of the small blood vessels and are then carried away by the blood current. If normal immunizing substances are present in sufficient proportion in the blood to retard the virulence of the pneumococcus sufficiently so that the white blood corpuscles can attack and destroy the pneumococci after they enter the blood, no infection of the circulatory system will develop. If, on the other hand, the pneumococcus possesses sufficient virulence, if it has surrounded itself with the ferment which it employs to digest the food on which it lives, in sufficient quantity and effectiveness to protect itself from attack by the leukocytes, the pneumococci will continue to grow and multiply in the blood until protective ferments or antibodies have been produced in sufficient quantity to cause their destruction. Wright calls pneumococci, streptococci and staphylococci serophites because they are capable of growing in the blood serums of the circulating blood. After the pneumococci have continued to grow in the blood for probably several days, at about the time the infection begins to localize in the lung, the patient usually has a chill followed by fever and other symptoms which mark the beginning of an active lobar pneumonia.

If the patient progresses favorably in the natural course of the disease, the pneumococci will disappear from the blood within a few days after lung consolidation has taken place. This would show that germ destroying protective substances have evolved sufficiently to destroy the germs in the blood and that in time the pneumococci involving the lung will also be eliminated. Protective germ destroying ferments or antibodies are

produced by the involved tissues during the infective process. During an infection, however, the central portion of the infected area is often so devitalized by the virulence of the infecting organisms that destructive processes with pus formation develop and if these tissues survive, it is because the tissues surrounding the central portion of the infected area—tissues that have come under the influence of the infection with less intensity—produce immunizing substances in sufficient quantity to eliminate the virulence of the infection and prevent destructive processes. So in cases of pneumonia where the pneumococcus is eliminated from the blood within a few days after lung consolidation develops, and since pneumococci meantime are found in great numbers in the deeper portions of the involved portions of the solidified lung tissue which is sparingly supplied with blood, the antibodies which are responsible for eliminating the pneumococci from the blood are produced by the involved lung tissues surrounding the consolidated portions of the lung. If, on the other hand, the pneumococci do not disappear from the blood after consolidation takes place, it indicates an unfavorable prognosis. In other words, adequate antibody formation is not taking place.

Now let us visualize the situation from an immunologic standpoint. From the time the pneumococcus establishes itself in the blood, it makes unhindered progress until lung involvement takes place. Then, if later on certain portions of the lung are favorably influenced by the infecting organisms, enough antibodies will eventually be evolved to overcome the infection; if not, the patient will die. The theoretic objectors to the use of vaccines in such acute infections contend that the patient already has an overdose of antigen in the form of a live infecting organism, then why inject killed organisms in the form of a vaccine? Dorland in his medical dictionary defines an antigen as "A substance that causes the formation of antibodies; a substance which has the power of inducing in the animal organism, under suitable conditions, the formation of antibodies." Evidently a pneumococcus which continues to grow and multiply until it destroys the life of the patient does not perform the function of an antigen. And even if the organism develops properties during the course of the infection which will cause the formation of antibodies, these properties certainly do not make their appearance until the infection has caused considerable damage. Evidently then, the all-important requirement is to supply the patient with a real antigen at the earliest possible moment so rapid antibody formation will take place and the infecting organisms become eliminated before destructive processes have time to develop. There is absolutely nothing pertaining to our immunologic knowledge that can in the least conflict with this fundamental principle. That killed organisms when injected into healthy tissues possess marked antigenic influences is so well established that further comment is unnecessary and

that such immunizing responses develop from killed organisms or vaccine injections during the course of an acute infection is a matter of clinical experience. This is readily explained. Live virulent organisms, as long as they exert destructive influences on the tissues with which they come in contact, can certainly not induce these tissues to produce antibodies, because the excessive toxic influence of the germ secreted ferments cripple these tissue cells in their defensive capacity. But when killed organisms are injected into healthy tissues, these tissues get busy to dispose of them and since the killed germs cannot produce toxic ferments to cripple the cells with which they come in contact, the entire cell energy can be devoted to the production of immunizing substances making the killed organisms or vaccines dependable antigens.

An objection to the use of vaccines in the treatment of such acute infections is based on the assumption that, since by this method the injected tissues must produce the antibodies before the therapeutic results can be expected, the process is too prolonged to be of practical value. From clinical results regularly obtained we know that this assumption does not hold good. Naturally the best results are obtained when the vaccine is applied early in the course of the disease. No one could expect prompt immunizing action from any antigen after the entire body has been saturated with germ produced toxins of comparatively long standing. We find that if a vaccine containing the various organisms usually found in respiratory infections or at least the various types of the pneumococcus, streptococcus and staphylococcus, is given within four or five hours after the initial chill, immunizing responses sufficient to cause a reduction of temperature to normal or near normal with corresponding other improved conditions will be found within eighteen to twenty-four hours, and, if the vaccine inoculation is repeated at daily or twice daily intervals in severe cases, recovery may confidently be expected with very few exceptions, within three to five days. In fact, if the vaccine is given early as suggested, typical lung consolidation seldom takes place. Such results certainly offer a conclusive demonstration that these vaccines possess antigenic properties which produce antibodies promptly.

The theoretic contention has been that if vaccines are employed at all in acute infections on account of the toxic conditions, treatment should be started with a small dose, but we find the reverse to be true. Acute conditions like pneumonia require large doses and short intervals and the more toxic the case the shorter the interval between inoculations. The usual initial adult dose of vaccines in extensive acute infections is 1.0 c.c. or 15 minims, repeated at daily intervals and in extremely toxic cases twice daily during the extreme toxic conditions, after that at 2 or 3 day intervals until recovery is complete.

This repeating of the inoculations at sufficiently short intervals is just

as important as the early application of the vaccine. This antibody production by means of vaccine injections is essentially a quantitative process. During the life process of the infecting organism, it produces ferments with which it defends itself by digesting the food it extracts from the available tissues. Some of these germ produced ferments become absorbed throughout the body. These tissue produced protective ferments or antibodies which develop from the vaccine injections combine with the ferments surrounding the infecting organisms and by this means rob them of their virulent properties so phagocytes dare to attack and destroy them. Some of these antibodies no doubt also combine with germ produced toxic ferments, which are present throughout the body and thus relieve the general toxic factor of the infection. But all this requires a quantitative proportion of tissue produced antibodies. If these tissue produced antibodies are all consumed before all the infecting organisms are eliminated, they may again begin to multiply and experience shows that this is just what happens; relapses take place, again followed by improvement after vaccines are again administered, but unfortunately this faculty to respond is sometimes lost if the relapse should take on serious proportions. For this reason, to be on the safe side, it is necessary to continue the inoculations at short intervals until the infection is brought thoroughly under control.

If the vaccine treatment is started after lung consolidation has taken place, the results are not so spectacular. While occasionally we precipitate a crisis by giving the vaccine, usually recovery takes place by lysis. While the results from the use of vaccine are not uniformly good when used late in cases of pneumonia, yet some apparently hopeless cases have shown distinct improvement within twenty-four hours after giving the vaccine with ultimate recovery. In this class of cases, there is great advantage in giving the vaccines in divided doses, 1.0 c.c. being given in three or four different parts of the body. In this class of cases, the free use of oxygen to prolong the patient's life until antibodies have time to develop, is of decided advantage.

What holds good with the use of vaccines in the treatment of lobar pneumonia also applies in broncho pneumonia and the pneumonias following epidemic influenza. In all these cases, vaccine treatment should be instituted at the earliest possible opportunity. Where the diagnosis is obscure, the patient should be given the benefit of the doubt just the same as diphtheria antitoxin is given in suspected cases of diphtheria.

Empyema

IN severe cases of pneumonia, pleurisy often develops with pus formation in the pleural cavity which requires drainage. Bacterial examination of the contents of the pleural cavity in these cases shows the pneu-

mococcus as the predominating organism. Streptococci, staphylococci and other organisms are also found. As a rule, after using vaccine in these cases during the early acute stages, the pus becomes very thin within a few days and then develops the appearance of serum. If, during this stage, the infecting organisms have disappeared, the drainage tubes may be removed and the opening allowed to close. In favorable cases, this may take place within five or six days after drainage has been established.

The same vaccine is employed as in the treatment of pneumonia. During the toxic stages it is given in 1 c.c. doses at daily intervals and after the toxic symptoms subside at 3 or 4 day intervals until recovery is complete.

In chronic cases that have been drained for a long time, any one of a large variety of organisms may be present. In addition to the streptococcus and pneumococcus, staphylococci, bacillus pyocyaneus, proteus, colon and tubercule bacilli are the most common. A bacterial examination of the discharge is necessary to make a diagnosis. The results in these cases of long standing are not so uniformly good. In some cases, autogenous vaccines will give results where stock vaccines have failed, and in others stock vaccines do better than autogenous. Not infrequently, however, indifferent results are obtained.

Pulmonary Abscess

A DETAILED description of pulmonary abscess formation is not necessary here. As a means of proper vaccine treatment, it is well to take into account the three principal conditions under which pulmonary abscesses develop: intense localized infection, pulmonary embolism and extension of an abscess through the diaphragm from the abdominal viscera.

Where pus accumulations exist, drainage is, of course, the first requisite, but to build up an immunizing resistance to limit the ravages of the localized infection is of equal importance. If the abscess is confined to the lung, the same infecting organisms usually found in respiratory infections are responsible and demand the same vaccine that is employed in empyema and broncho-pneumonia.

In cases where the abscess has its origin in the appendix or some other abdominal organ and has broken through the diaphragm, the colon bacillus is almost invariably the principal offender and should be contained in the vaccine. If the abscess has broken into a bronchial tube and the pus is being coughed up, a bacterial examination will readily indicate what vaccine should be employed or an autogenous vaccine prepared.

Pneumonia Prophylaxis

MUCH has been accomplished toward preventing pneumonia by prophylactic immunization. This is best done by injecting three or four doses of a mixed polyvalent vaccine. This procedure is particularly applicable in large industrial plants especially to prevent pneumonia during the prevalence of influenza. Formula 38 is admirably adapted for this purpose. This vaccine was employed for this purpose in many thousands of cases during the epidemics of 1918 and 1920, resulting in a mortality rate of but one in two thousand. To employ prophylactic immunization against pneumonia as a routine proposition during normal times does not appeal to the general public. Most people disregard the possibility of contracting a disease like pneumonia and consequently don't see the importance of procuring protection through prophylactic immunization. There is another condition, however, where prophylaxis against pneumonia can be universally applied without the least objection and that constitutes the treatment of the minor respiratory infections called colds with vaccines. These colds are very amenable to vaccine treatment. Usually the acute symptoms subside within twenty-four hours after the first inoculation and by repeating inoculations at 2 to 3 day intervals for three or four injections, the cold is entirely eliminated and the many sequelæ, such as pneumonia, broncho-pneumonia, mastoiditis, endocarditis, cholecystitis, nephritis, etc., will be avoided. In the treatment of colds, vaccines should be employed. Treatment is usually started with 0.2 c.c. and the dose gradually increased to 1.0 c.c. and the rate of increase will depend on the amount of reaction that develops after each inoculation. The dose should be so gauged that marked reactions are avoided. Inoculations are usually made at 2 to 4 day intervals.

PROCTITIS

INFECTIONS of the rectum are most commonly due to the colon bacillus and staphylococcus. Mixed infections with the streptococcus and other organisms are frequently found. Local treatment and operative procedures are usually indicated but the infection can more readily be brought under control by therapeutic immunization in conjunction with the other treatment. A combined colon-bacillus vaccine (Formula 35) is usually indicated. The infection being subacute or chronic, treatment is started with the usual dose 0.2 c.c. and then worked up to 1 c.c. Inoculations in the more acute varieties are made at 2 to 3 day intervals and in the chronic cases, 5 to 7 days apart.

PROSTATITIS[1]

PSORIASIS[2]

PUERPERAL FEVER[3]

PYORRHEA

PYORRHEA is due to an infection of the peridental membrane with a resulting absorption of the alveolar process, retraction of gum, and final loss of tooth unless the infective process is arrested.

Much bacteriological work has been done to determine the exact etiologic factor in this disease. The usual pyogenic organisms, streptococci, pneumococci, staphylococci and other germs usually found in infective processes of the mouth, are found in the pus procured from scrapings in the space around the teeth.

The entamœba buccalis has been considered a possible etiologic factor in this disease for some years. Smith and Berrelle, at a meeting of the Pennsylvania State Dental Society, July, 1914, announced that as a result of their investigations they considered this organism the real cause of the disease. About the same time and a little later, Bass ("Alveolar Pyorrhea," p. 22) found the entamœba buccalis in 300 cases of unquestioned pyorrhea, while the organism was not found in control cases. He considers the entamœba buccalis the real cause of the disease, because of its constant presence and from the clinical symptoms of improvement after killing of the organism with the use of emetin, one of the alkaloids obtained from ipecac, which has a specific poisonous effect on the entamœba buccalis.

From this viewpoint, the pus organisms always found in the diseased tissues would be secondary invaders, entering after the entamœba has destroyed the peridental membrane. Bass is of the opinion that these organisms cling to the entamœba buccalis and are carried down into the tooth socket with them. He contends that entamœbæ, by their continuous motile activities, disturb the granulating surface in the alveolar process and by this means dig up new soil, as it were, for the deeper penetration of the pus organisms, with a resulting gradual destruction and absorption of the alveolar process.

At all events, from a careful study of this disease, it must be quite clear that the diseased condition is due to the combined activities of the entamœba buccalis and pyogenic organisms and that neither of these factors would cause the same amount of destruction when operating alone. This fact, to my mind, has been clearly brought out by the immunizing and the emetin methods of treatment.

[1]See Gonorrhea
[2]See Eczema
[3]See Gynecological Infections, Blood Infections and Gonorrhea.

It can readily be seen that, where a comparatively low resistance to streptococci or other pyogenic organisms exists, more rapid progress of the disease will take place under the combined influence of the entamœba buccalis and the pyogenic organisms than where the pus organisms could not maintain themselves on account of a high immunizing resistance to them. In fact, there is good reason to believe that the entamœba could not maintain itself, especially in the early stages of the disease, if the pus-producing organisms were not present as accomplices. The good results obtained from the use of vaccines in the treatment of pyorrhea, especially when used in the early stages, demonstrates this. In our own experience, we have seen well-advanced cases cured with the use of vaccines. The good results from the use of vaccine in pyorrhea were recently seen in one of our employees. In this case the pyorrhea had been fairly well advanced. A dentist was consulted who took care of the teeth by the usual methods of cleansing and scraping and without his knowledge vaccine inoculations were given at the same time. The case improved rapidly and the dentist was surprised at the progress that was being made. In three months' time the pyorrhea was relieved without any apparent return of the disease.

From the results obtained in the treatment of pyorrhea with vaccines, the pathogenicity of the pyogenic organisms associated in the infection becomes evident, and, furthermore, the apparently permanent results that are secured also indicate that the entamœba buccalis cannot successfully maintain itself in the peridental membrane when the soil is unfavorable for the growth of pyogenic organisms, especially so in the early stages of the disease.

The unquestionable good results that have been obtained from the use of emetin hydrochloride, hypodermically or in the pus pockets, as shown by Bass and others, is conclusive evidence of the pathogenic character of this organism in pyorrhea. Bass has found that in practically all cases the entamœba disappears from the tooth sockets after a week's treatment with emetin. Concerning the results procured, Bass ("Alveolar Pyorrhea," p. 137) says:

"Though the specific emetin treatment causes the disappearance of demonstrable entamœbæ, the lesions or pockets remain and will require days, weeks, or months to heal, depending largely upon the size, extent and nature of the individual lesions as well as upon the natural healing powers of the individual patient. In many lesions there is considerable alveolar bone denuded of its periosteum, which, therefore, must be removed by the long, slow process of nature, if not aided by artificial, mechanical means. It requires nature several months also to remove the alveolar bone above the level of living peridental membrane in the case of pyorrhea. After the entamœba have been destroyed and the blood

no longer contains emetin, these lesions or pockets offer the most favorable soil for reinfection."

It should be remembered that emetin, in the doses given to destroy the entamœba has practically no germicidal effect on the pyogenic cocci, and here the natural healing power of the patient depends largely on his ability to cope with the pus organisms present in the alveolar process and tooth sockets. That vaccines will aid the "healing powers" in the presence of an infection has been sufficiently demonstrated.

From these various considerations, it would appear that the most rational procedure would be to employ emetin to get rid of the entamœba buccalis and vaccines to hasten the healing process by immunizing against the pyogenic organisms.

Emetin hydrochloride is marketed by drug houses in sealed ampules containing one-half grain each, ready for use. The contents of the ampule are withdrawn into the syringe and injected intramuscularly, the usual antiseptic precautions being observed. Daily inoculations for one week will suffice. Where extensive pus pockets exist, it may be necessary to flush them with emetin solution. For this purpose, emetin hydrochloride 1:10,000 will answer the purpose.

Vaccine inoculations should be made by employing a vaccine corresponding to the organisms present in the pyorrhea pockets, either stock or autogenous, usually streptococci, pneumococci, staphylococci and micrococcus catarrhalis, (Formula 40), 0.2 or 0.3 c.c. the first dose. The dose should be repeated at 5 or 7 day intervals and the dose gradually increased to 1 c.c. or more and the treatment continued until the entire inflammatory process is relieved.

There has been much said and written concerning the importance of salivary calculus as an etiologic factor in pyorrhea. From our knowledge of germ activities in the production of renal calculi and gall stones, there is no room for doubting that salivary calculi are the direct cause of deposits from pus formations. These salivary calculi should be carefully removed, because they are a direct source for a continuous reinfection and also mechanically irritate the gum.

Pyogenic bacteria complicate pyorrheal infections and aid in the breaking down of body resistance, thereby lowering the local and systemic immunity. To resist the invading pyogenic bacteria, it is necessary to increase the defensive and recuperative power of the body and establish immunity.

Therapeutic immunization with polyvalent bacterial vaccines in Alveolar pyorrhea have passed the clinical test as recognized therapeutic immunizing agents. The treatment of pyorrhea with polyvalent vaccines stimulates the metabolism and defense of the body which is necessary in overcoming the infection.

PYEMIA[1]

RECTAL FISTULA[2]

PYELITIS

WHENEVER pus is found in the urine, a careful search for tubercle bacilli should not be neglected, and, if found, special treatment for a tubercle infection of the kidney instituted. In the absence of a tubercular infection, the usual infecting organisms are the colon bacillus, streptococci, staphylococci and pneumococci. Occasionally we find the bacillus pyocyaneus. It is difficult to say just how these infections develop, whether the infecting organisms lodge in the pelvis of the kidney while they are being thrown off by this organ or whether the infection extends from the bladder to the kidney through the ureter.

Whether bacterial examinations show a straight colon bacillus infection or a mixed infection with the common organisms mentioned above, a combined colon bacillus vaccine containing these various organisms (Formula 35) is preferably employed because sooner or later it is liable to become a mixed infection if not cured in time. Treatment is usually started with 0.2 c.c. and the dose gradually increased to 1 c.c. or more. If the case is acute, as is often the case during pregnancy, inoculations should be made at 1 to 2 day intervals, and the dose rapidly increased to 1 c.c. especially if no material reactions develop from the smaller initial doses. The results in these cases of pyelitis in pregnancy are remarkably good. Bacterial examination of the urine should be made at least every few weeks to determine the presence of bacteria. Treatment should be continued until the urine is free from infecting organisms.

In cases of pyonephritis, the same vaccine is employed, but the kidney also being involved, it is necessary to employ measures toward aiding elimination the same as in cases of nephritis.

RHEUMATISM

Rheumatism (Gonorrheal)[3]

RHEUMATISM is now generally regarded as being an infective arthritis. The fact that the removal of an infected tonsil or some other focus of infection was often followed by improvement or recovery of arthritic joints led many to believe that the joint involvement was due to toxic materials that gained entrance into the general circulation from the infected area. Rosenow's work (Journal A. M. A., September 12, 1914), however, where he succeeded in isolating pathogenic organisms from the tissues of all classes of rheumatic joints conclusively demon-

[1] See Blood Infections.
[2] See Abscesses.
[3] See Gonorrhea.

strates that in rheumatic arthritis the infection actually exists in and around the joints themselves; the tonsil or other focus of infection merely serving as a port of entry from where the blood conveys the germs to the joints. Billings (Journal A. M. A., September 12, 1914), says: "The focus of infection may be located anywhere in the body. The usual site is in the head, in the form of alveolar abscess, deep tonsillar or peritonsillar abscess and chronic sinusitis. Cholecystitis, acute or chronic appendicitis, submucous abscess anywhere, salpingitis, vesiculitis, seminalis, prostatitis, etc., are examples of the local conditions. Furthermore, secondary foci in lymphnodes proximal to the primary focus and to systematically infected joints, muscles, etc., become additional sources of continued and more general infection. 'Overdentistried' teeth may cause or prolong alveolar disease. Tonsillotomy may add a sealing scar to the infected tonsillar stumps."

The presence of a focus of infection always constitutes a lowered resistance to the causative infecting organisms otherwise the local infection could not exist. This lowered resistance, in turn, makes it possible for germs that gain entrance to the blood stream from the infected focus to grow elsewhere, and the surgical removal of such a focus does not necessarily raise the immunizing resistance to the infecting organisms, nor does the surgical treatment of the focal infection eliminate the infected areas already established as joint involvements. Furthermore, in many cases of arthritis, the original focus of infection becomes entirely eliminated while the joint involvements continue. In the treatment of arthritis, the surgical treatment for the relief of pus accumulations is very important, but unless treatment is instituted which adequately raises resistance to the germs which cause the arthritis, not much permanent relief should be looked for.

The streptococcus or strepto-pneumococcus group of organisms are the most common invaders. H. Greely (Medical Record, June 1, 1914) regards all arthritis inflammations as due to infection and ninety per cent of them caused by the streptococcus. Acute inflammatory rheumatism, chronic articular rheumatism and arthritis deformans, he considers as being due to the same cause but modified by the varying susceptibility of different individuals which determines the duration and severity of the disease.

The streptococcus is an unstaple organism and sometimes changes from one type to another during the course of an infection. Rosenow has even succeeded in converting certain types of the streptococci into pneumococci and pneumococci into streptococci. Staphylococci, colon bacilli and other organisms also appear to be responsible for joint inflammations and no doubt, mixed infections exist in many cases.

Recognizing the infectious character of the various forms of arthritis,

therapeutic immunization at once suggests itself as the proper procedure. Bacterial vaccines have so far proven themselves as the most efficient agents to this end. In the selection of a vaccine some advocate the use of an autogenous vaccine prepared from the principal infecting organisms found in some focus of infection. While unquestionable good results have been obtained by this method, yet it should be remembered that the organisms found in a focal infection do not necessarily correspond to the ones causing the arthritis. This original focus of infection from which the germs causing the arthritis originally migrated may entirely disappear and some new focus subsequently develop which has no connection with the existing arthritis. Furthermore, even in cases where the original organism is still present it may have become so modified and attenuated that it no longer is of special value as an immuno producer in the form of a vaccine. It is not an uncommon experience in chronic infections to find that polyvalent stock vaccines give results where autogenous preparations fail. This is in all probability due to a mutual tolerance which, in time, develops between the tissue cells and the infecting organisms. If a vaccine prepared from such an organism is injected the same amount of tissue activity is not aroused as would take place from a stock vaccine prepared from active virulent organisms of the same type. Extensive experience shows that the best results are obtained from the use of polyvalent stock vaccines and mixed vaccines are better than single organism preparations.

In making a diagnosis of rheumatic arthritis, it is very important to exclude a possible suppurative osteomyelitis, tuberculosis of the joint or a gonorrheal infection. Acute rheumatic arthritis is sufficiently distinctive in its clinical symptoms. Endocarditis is such a frequent complication in acute arthritis that its presence should never be overlooked. Early treatment is of utmost importance because if an immunity is established early, heart complications will be avoided. Wolverton (Merck's Archives, July, 1914) says: "In those cases in which I have used the 'Vaccine treatment' before there was cardiac involvement, no such involvement took place subsequently; any agent which has such a prophylactic value should at once commend itself. And this treatment is free from danger." In acute arthritis, a polyvalent stock streptococcus vaccine has been extensively employed but later experience shows that it is better to employ a combined streptococcus, pneumococcus, staphylococcus preparation (Formula 6). The streptococcus and pneumococcus are very closely allied organisms and evidently some cases of arthritis are due to a pneumococcus. By using the combined vaccine, infections by this organism are taken care of. Treatment should be started by giving the usual dose and repeating at comparatively short intervals, the same as in other acute infections. In severe cases where there is considerable

temperature daily inoculations for several days are advisable. Improvement will be observed after the first or second inoculation as indicated by relief from pain and a reduction of temperature. After improvement is observed, treatment should be extended to three or four day intervals. In these acute cases, not much reaction follows the inoculations and for that reason the dose may be rapidly increased to 1.0 c.c. or more. Some new joints may become involved with severe acute symptoms but they will soon subside under the vaccine treatment. Infants and children are very amenable to this treatment and should receive from ¼ to ½ the adult dose. Treatment should be continued for several weeks at five to seven-day intervals after all symptoms of the disease have subsided to guard against relapses.

Subacute and chronic arthritis present themselves in an endless variety of forms. Some cases become chronic as the result of repeated uncured acute attacks while others come on insidiously and present chronic tendencies from the start. In these subacute and chronic cases, we find that an extensively mixed vaccine containing streptococci, pneumococci, staphylococci and colon bacilli (Formula 35) gives the best results. Treatment should be started by giving the usual initial dose 0.2 c.c. or 3 minims, but must be given at longer intervals than in acute cases. From four to seven day intervals is often enough. Reactions from the vaccines are more marked here than in acute cases. Where considerable local irritation develops at the point of inoculation, the dose has been too large and should be followed by a smaller one. Where no material disturbance follows an inoculation, the dose may be rapidly increased to 1.0 c.c. or more. Many cases show marked improvement after the first inoculation but others improve more slowly. In these chronic infections there is, as a rule, no advantage in crowding the treatment. Much better results may be looked for by persistently continuing the treatment for several months. This is particularly true of the deforming types of arthritis. These cases have a tendency to steadily grow worse, not being much influenced by drugs, baths, or local applications. Vaccine inoculations, however, will benefit them if the treatment is carefully followed up for a long period of time. Many cases will not show much improvement for three to six months but little by little some advantages will be gained. Treatment should be continued for a year or more. The first noticeable improvement will consist in the patient's appetite being better and his taking on flesh. With this general health improvement the joints also get better. Even if nothing more than staying the progress of the disease is accomplished, this in itself is worth while. With the proper application of vaccine therapy early in the course of the disease, the horrible deformities sometimes met with would be avoided.

RHINITIS, PHARYNGITIS, SINUSITIS

MOST infections take place by microbic invasions of mucous membranes. The respiratory tract and mouth offer an extensive area of mucous membrane which is constantly exposed to attack by germs that may be present in the inhaled air or adhere to partaken food, and this makes infections of this part of the body most common. In fact, a large portion of the minor ailments met with in everyday practice and many serious diseases as well have their origin in the nose, throat or mouth. Acute rhinitis, pharyngitis, laryngitis or tonsillitis may be regarded as a trivial affair which usually subsides sooner or later without serious consequences, but dangerous extensions of infections from these small foci take place entirely too often to justify our neglecting them from the standpoint of immuno-therapy.

In a patient who for some time has complained of slight fever associated with an erratic heart action, endocarditis is at once suspected, and if verified the trouble is usually traced to a tonsillitis or similar infection. The same may be said of rheumatic fever. Mastoid infections and otitis media with few exceptions have their origin in the throat. Sinus infections also have their origin in extensions from the nasal mucous membrane. Bronchitis and broncho-pneumonia follow "colds," and lobar pneumonia have the same origin. The clinical history in cases of nephritis often shows that the disease had its origin with a respiratory infection, when infecting organisms unquestionably gained entrance to the general circulation and caused metastatic infections involving the kidneys. Gastric ulcers in all probability are also due to metastasis produced by germs that gained entrance to the circulation from localized infections of the mouth or respiratory tract. When infections in the mouth, nose or throat exist a large number of the germs are constantly swallowed and may start localized infections in the various portions of the digestive tract.

Among the common ailments met in general practice, acute infective processes of the upper respiratory tract respond most promptly to vaccine therapy. Few escape rhinitis, pharyngitis, laryngitis, "colds," but results from the use of medicines are so disappointing that comparatively few people consult a physician when thus afflicted. The impression that "nothing can be done for a cold" is quite prevalent because no definite method of treatment for these cases has been adopted by the medical profession as a whole. This inefficiency in the treatment of minor ailments has lowered the medical profession in the estimation of many well-meaning, intelligent laymen. The argument is often advanced that if a doctor can not cure so trivial an ailment as a cold, how can he accomplish anything when confronted with a serious disease. Naturally the

physician who is able to give prompt and efficient relief when called on to treat minor ailments soon gains the confidence of his patients in the more serious troubles; and what is true of this esteem toward the individual physician applies equally to the medical profession as a whole. Probably 75 per cent of the prevailing infections are simply tolerated by the laity until spontaneous recovery takes place; often the infection, meantime, becomes chronic, being unaided by a physician, simply because nothing sufficiently tangible is offered to warrant taking the treatment. Most people have found that throat lozenges or rhinitis tablets, at a cost of 5 or 10 cents, will give about as much relief as a prescription from a family physician, but we all know how sadly inefficient these remedies are. If efficient treatment were administered these neglected ailments would be regularly taken care of by the medical profession, to the enormous benefit of the general public. Few people would tolerate a "cold" if they were aware of the prompt relief and efficient cures that may be obtained from the injection of bacterial vaccines by their physician.

Much careful bacteriological research work has been done by many investigators to determine the responsible infective agent in these respiratory infections commonly called colds. A distinction must be made between the early acute condition and the later stages and complications. Pathologists have for a long time contended that the early acute symptoms of a rhinitis do not conform to symptoms which are produced by pneumococcus and streptococcus infections. We also find that patients receiving a mixed vaccine practically identical to the one employed in the treatment of respiratory infections for chronic arthritis, for example, will develop an acute rhinitis while receiving vaccine inoculations but this rhinitis will disappear in a few days. This would indicate that while the patient is immune to pneumococci, streptococci, etc., there is a susceptibility to an infection which is responsible for these acute symptoms. So, most pathologists have come to the conclusion that the early acute symptoms of acute coryzas are due to an unknown organism probably a filtrable virus. This primary invader really serves the purpose of paving the way for pneumococci, streptococci, staphylococci and other organisms which in turn become the real offenders; being responsible for prolonging the infection, causing involvement of the sinuses, middle ear, mastoids, etc.

From this viewpoint it is perfectly clear that bacterial vaccines will not absolutely prevent these acute infections but will shorten their course and prevent complications. The pneumococcus, streptococcus, staphylococcus, micrococcus catarrhalis, influenza and Friedlander bacillus are the most common secondary invaders and are usually found in association.

In the fresh acute cases of rhinitis or bronchitis we are dealing with the primary infection and aim to develop an immunity in time to prevent the more serious infection by pneumococci, streptococci, etc. Here, as a routine measure, vaccine Formula 40 or 38 should be injected, beginning with 0.2 c.c. and rising, at intervals of two or three days, to 1.0 c.c. If, after a few injections, the acute symptoms have subsided, but the trouble continues with considerable mucus discharge, inoculations should be continued at three to five-day intervals. Where there is a copious discharge associated with a disagreeable odor the Friedlander bacillus is liable to be present, when Formula 36 should be employed.

Subacute or chronic cases of catarrh—such as occur in patients in which the condition is quiescent for a greater part of the year and only lights up occasionally—call for the administration of Formula 40 or 38. If, however, they are characterized by an abundant secretion of mucus, the bacillus of Friedlander is probably present, and vaccine Formula 36 is best given. The dosage is 0.3 c.c. increased to 1.0 c.c. at intervals of from four to seven days.

Some people suffer from recurrent attacks of respiratory infections because no lasting immunity develops from a spontaneous recovery from the infection. In such cases a lasting immunity can be developed by treating the infection during the acute stages with vaccines and continuing the treatment for several months with injections at weekly or biweekly intervals. Another attack may develop in time but as a rule it is not so severe and will yield promptly to further vaccine treatment.

The results from the use of bacterial vaccines in the early acute stages are quite striking. As a rule relief is obtained within one or two days. If the vaccine treatment is not continued, however, the case is liable to relapse when the acute symptoms reappear. After the infection is brought under control injections should be continued at three to four-day intervals until all the symptoms have subsided.

SINUS AND ANTRUM INFECTIONS[1]

SINUS and antrum infections are due to extensions of the infection from acute nasal catarrh and naturally are due to the same organisms and from a standpoint of immuno-therapy require the same bacterial vaccine treatment. From the fact that sinus infections when once established have a tendency to become chronic it is of utmost importance to have these infections cleared up as rapidly as possible. While instituting vaccine treatment it is also very important to make a careful examination to determine abnormalities which require surgical treatment. Proper drainage must be established and maintained and where antrum infections are due to an infected tooth socket the tooth should be extracted. A large majority of these cases are due to the common respiratory infecting

[1]See Rhinitis and Colds.

organisms but occasionally the bacillus pyocyaneous, colon bacillus, and pseudodiphtheria bacillus are found. In the treatment of these cases a corresponding stock or autogenous vaccine should be employed.

Prophylaxis[1]

MANY people are subject to taking colds. In such cases it is advisable to employ prevention. This is effectively accomplished by giving combined vaccine Formula 40 at weekly intervals, starting with 0.5 c.c. and increasing to 1.0 c.c. for three or four inoculations about three times during a year.

This, however, does not absolutely prevent contracting a cold, but it is found that if a cold is contracted, it will be of short duration and especially so if a few doses of the vaccine are given at two to three day intervals during the attack. In many instances it is necessary to give smaller doses at daily intervals for relief.

SALPINGITIS[2]

SCARLET FEVER

THE unusual prevalence of scarlet fever demonstrates the inadequacy of isolation and disinfection as an efficient means of controlling infectious diseases. That the streptococcus is the important active pathogenic agent in this disease has been conclusively demonstrated by Schleissner (Wiener Klinische Wochenschrift, April 95, 1910), who found streptococci in practically pure cultures on the tonsils during the very early stages of nearly all scarlet fever cases. He also found streptococci in the blood in a large proportion of the 73 cases examined.

The streptococcus found in cases of scarlet fever is the same, in cultural characteristics and other properties, as streptococci found in cases of epidemic sore throat and from other sources. This was forcibly brought out in a paper by Drs. Wohl and Detweiler (Interstate Medical Journal, Sept., 1916), in which they show identical characteristics of streptococci isolated from epidemic sore throat and scarlet fever cases. In their agglutination tests they found that blood serum obtained from convalescent cases of scarlet fever agglutinated streptococci isolated from cases of scarlet fever, streptococcic fever or from a felon. Blood serum obtained from convalescent cases of streptococcic fever also agglutinated streptococci isolated from scarlet fever cases. These findings conform with the results of other investigators, both in this country and abroad. Nothing has developed which would indicate that the streptococcus isolated from cases of scarlet fever possesses any specific characteristics.

That prophylactic immunization is the most effective measure in controlling infectious diseases has been conclusively demonstrated by immu-

[1] See Rhinitis and Colds and Pneumonia also.
[2] See Gonorrhea in Women

nizing in typhoid fever, cerebral spinal meningitis, cholera, bubonic plague, and other diseases. Since the streptococcus is the dangerous pathogenic factor in scarlet fever, prophylactic immunization to this organism is the most scientific and rational procedure.

Concerning scarlatina prophylaxis, Wohl and Detweiler say: "For practical purposes, however, we must admit that the streptococci play the most important role in the clinical entity called scarlet fever."

Once this is realized, proper attention to the destruction of the streptococci, either locally by disinfection of discharges from the nose, throat and ear, or by raising the constitutional resistance against them by vaccination, would certainly lessen the incidence of the disease. The work of Gabritschewsky, and his other Russian associates, in immunizing with streptococcic vaccine the children exposed to scarlatina, is conclusive that it has a decided value from a prophylactic standpoint. A number of his fellow countrymen pursued a study along these lines, although but few have taken up the matter in this country.

Smirnof observed that of 91 unvaccinated children 37.3 per cent. developed scarlet fever, and of 12 vaccinated children 3.93 per cent. developed it. The protection by repeated injections is shown by the following table:

Vaccinated	Cases	Incidence
Once	1,295	1.69
Twice	1,018	0.19
Thrice	256	0.00

Kogan reported the vaccination of 62 children in an asylum during an epidemic of scarlet fever. The children remained immune from 1908 to 1911, when a new epidemic broke out, and of these 62 vaccinated cases, only 2 contracted scarlet fever, or 3 per cent. while out of the 26 new non-vaccinated cases admitted to the asylum, 8 contracted the disease or 30+ per cent.

Watters reports the successful immunization of nurses with streptococcic vaccine. Of those vaccinated, only 2.7 per cent. contracted the disease, while of the non-vaccinated 35.7 per cent. acquired the disease.

To effectively protect against scarlet fever three doses of streptococcus vaccine should be given at five-day intervals. Formula 42 is admirably adapted for scarlet fever prophylaxis. It is polyvalent in composition and made up in proper suspension for convenient adjustment of dosage. The first dose should be 0.3 c.c., second dose 0.5 c.c. and third dose 1. c.c.

We will admit that prevention is better than cure but since there are many cases of scarlet fever, the importance of treating them with bacterial vaccines should not be overlooked. It is the consensus of opinion of all those who have used bacterial vaccines extensively, that the best

results are obtained when they are employed in the early stages of acute infections. In streptococcus infections the greatest amount of irreparable damage is done during the early active stages of the infection; before the immunizing mechanism has had a chance to respond in immuno production. Live virulent streptococci do not influence tissue cells favorably for rapid antibody production, whereas killed streptococci—streptococcus vaccine—when injected into healthy tissues have a favorable influence on tissue cells for rapid antibody formation. In other words, tissue cells respond more rapidly in establishing an immunity under the influence of killed organism injections than where exposed, unaided to the devitalizing influence of the live virulent organisms. For this reason, early treatment is very important. By early vaccine treatment, tissue cells are actively influenced for antibody production and by this means, enough antibody will be produced to stay the progress of the infection sufficiently to prevent serious complications.

The staphylococcus is frequently a complicating factor in localized streptococcus infections in scarlet fever. For this reason it is well to use a streptococcus, staphylococcus combined vaccine in the treatment of scarlet fever. A streptococcus combined vaccine (Formula 10 or 6) is favorably employed. Treatment should be started as soon as possible, repeating inoculations at daily intervals and in extremely toxic cases the vaccine may be given twice daily. After the toxic symptoms have subsided, inoculations should be extended to 3 or 4 day intervals until the patient has recovered. The dose for adults is 1 c.c. Children should receive from one-fourth to one-half this amount.

SCIATICA[1]

SINUSITIS[2]

SKIN INFECTIONS[3]

SURGICAL PROPHYLAXIS[4]

BACTERIAL Vaccines properly administered form valuable adjuncts and prophylactors in major and minor operative surgery.

The beneficial results of surgical interference in inflammatory conditions associated with pus formation have been so generally recognized that many operators consider their duty in such cases ended when adequate drainage has been established. A self-satisfaction that everything possible has been done is often a great hindrance to progressive work. In operating on cases where pus exists there is always danger of the infection extending into the tissues opened up as a result of the operation. Many times pus cavities are deep-seated and extensive

[1]See Neuritis.
[2]See Rhinitis.
[3]See Furuncles, Eczema, etc.
[4]See Wound Infections.

operating is necessary to reach the seat of trouble. In all such cases the immunizing influence of vaccines is of unquestionable value. Many operators recognize the value of vaccines in septic wounds and give them after clinical symptoms indicate that the infection has extended. In a publication we notice that a surgeon had an autogenous vaccine prepared from streptococci and colon bacilli isolated from the removed appendix to be given to the patient "in case he needed it." Here is a case where the infection existed and if vaccines are of any value he needed it before clinical symptoms indicated a post-operative extension of the process to avoid such extension. A better method still is to give the patient a stock vaccine corresponding to the probable infecting organisms just after or preferably before and after the operation. This will avoid the necessary delay incidental to making autogenous vaccines and the patient will obtain the benefit of early treatment. This method has given us such uniformly satisfactory results that we can unhesitatingly recommend it as a routine procedure.

Vaccines are advantageously used in major wounds from severe trauma, this includes compound fractures, etc., etc. Here the tissues have been cut, bruised and lacerated without the aseptic precautions observed on the operating table, making infections always more or less liable to occur. To give antitetanic serum when the wound was made under conditions making tetanus infection imminent is now recognized as a rational procedure. In accidental injuries staphylococcus and streptococcus and frequently infection by both organisms is always possible, and to give a prophylactic dose of combined streptococcus-staphylococcus vaccine is just as reasonable as the tetanus prophylaxis above referred to.

Through the influence of Sir A. E. Wright, millions of doses of "mixed infection vaccine" have been prepared in St. Mary's Hospital, London, and in the British Government laboratories, and used in the army hospitals of England and France with the result of materially reducing the dangers of the common pus infections in innumerable wounds.

Bacterial vaccines are more and more coming into use as prophylactors in operative cases where no indications of infective processes exist. It will not be long before the prophylactic vaccine inoculation will become a part of pre-operative routine just as the blood count and the urinary test are. The absolute harmlessness of the procedure is unquestioned, and the only thing that must be overcome is the conservatism of certain members of the profession. Such conservatism, however, cannot prevent the final recognition of the fact that vaccines may be advantageously used as prophylactors in surgical work.

In abdominal surgery prophylactic immunization should be instituted

prior to every operation, by the administration of a mixed stock vaccine containing the principal organisms found in abdominal infections. These comprise the streptococcus, the colon bacillus, the pneumococcus, and the staphylococcus. The procedure is absolutely harmless and can accomplish much good by raising the immunity and thereby preventing dangerous post-operative infections or extension of existing infections.

TONSILLITIS
Both Acute and Chronic

INFECTIONS of the tonsils are common. Here the streptococcus is the most common invader. In making a clinical diagnosis of tonsillitis, the fact, that a membranous exudate resembling diphtheria is often found to be due to streptococci, should never lead one to neglect giving diphtheria antitoxin at once where a reasonable suspicion exists that the case may be one of diphtheritic infection and have the diagnosis verified by bacterial examination. If the symptoms indicate severe infection, a vaccine should be given in conjunction with the antidiphtheritic serum, because by this means active immunization will be hastened toward eliminating streptococcus involvement while the antitoxin is establishing a passive immunity toward a possible diphtheria infection. Furthermore, complicating infections by streptococci in diphtheria are not uncommon and by using a streptococcus vaccine in conjunction with diphtheria antitoxin a definite purpose is served. We are confident, as a result of clinical experience, that in many cases of diphtheria where the inflammatory condition is extensive, involving lymphatic glands, the streptococcus is an important complicating factor which will be relieved by employing streptococcus vaccine in conjunction with antidiphtheritic serum. The same holds good with extensive throat infection with lymphatic involvement in cases of scarlet fever.

While most cases of tonsillitis are due to streptococci, yet in some cases the pneumococcus is found, and the staphylococcus is commonly associated probably as a secondary invader. The micrococcus catarrhalis is so often found in crypts of inflamed tonsils that this organism may also be regarded as a pathogenic factor.

From the bacterial flora of tonsillitis, it is clear that the same combined vaccine employed in respiratory infections (Formula 6 or 40) also applies here. The initial dose should be gauged by the severity and extent of the infection. Cases with fever and lymphatic involvement should receive 1 c.c. and the dose repeated at 1 or 2 day intervals. In less severe cases, treatment is started with 0.3 to 0.5 c.c. If treatment is started early, before a necrotic center has developed, the infection may be aborted without pus formation. Usually marked relief is obtained within one or two days, when a rapid recovery will follow.

The importance of applying immuno-therapy in acute tonsillar infections cannot be overestimated when we consider the serious complications which so often follow these cases when allowed to run the usual course. Heart infections, acute rheumatic arthritis, nephritis, appendicitis, and gall-bladder infections only too often have their origin in tonsillitis. By treating the primary infection through the immunizing method with bacterial vaccines, these secondary complicating infections are avoided.

Repeated infections of the tonsils disorganize them with a resulting enlargement and increased susceptibility to repeated infection. Such tonsils can serve no useful purpose and should be dissected out as soon as the acute infection has subsided. Such tonsils are always an open gateway to infections and are liable to lead to serious consequences.

TUBERCULOSIS

THE vaccine treatment of tuberculosis assumes two distinct phases: Immunization towards controlling the tubercle infection and immunization to overcome infections by pyogenic organisms, which almost invariably complicate tubercle lesions.

The treatment of tuberculosis by the immunizing method has received an unusual amount of continuous attention from the time Koch brought out his tuberculin, twenty-eight years ago. To Sir A. E. Wright, however, deserves the distinction of having placed therapeutic immunization in tubercle infections on a scientific basis. By means of his opsonic index, he demonstrated that tuberculins were employed in doses entirely too large to obtain immunizing responses.

As a whole, there can be no doubt but that tuberculins are of therapeutic value when carefully employed so as to avoid focal reactions and especially when used in combination with bacterial vaccines to combat mixed infections.

The toxic properties in tuberculins are in all probability due to something contained in the virulent tubercle bacilli. This objection has been overcome by our employing a non-toxic strain of tubercle bacillus in the production of Sherman's Non-Virulent T. B. Vaccine, Formulas 45 and 47.

This tubercle bacillus has been so attenuated that the injection of large doses of the live organism will not cause infection in guinea pigs and yet a vaccine prepared from these same tubercle bacilli when injected subcutaneously will stimulate efficient antibody formation for immunizing purposes as shown by animal experiments and the favorable results obtained in clinical cases.

On account of its non-toxic character, this Non-Virulent T. B. vaccine is applicable in all stages of tubercle infection. Naturally, the best results are obtained in the early stages, where uniform good results may

confidently be expected. In moderately advanced cases, the results are also good, and, if treatment is persistently carried out, a large majority will be clinically, and apparently permanently, cured. In advanced cases the combined Non-Virulent T. B. and mixed vaccine treatment will certainly give much relief, and in some cases will prolong life.

In the treatment of tuberculosis, immunizing efforts must be directed simultaneously towards the tubercle infection with the Non-Virulent T. B. vaccine and the pyogenic infection with a mixed vaccine. This is most effectively accomplished by giving the tubercle vaccine alternately with the mixed vaccine.

This avoids the possibility of confusing reactions. If the mixed vaccine is injected with the tubercle vaccine, it is impossible to know if the reaction is due to the tubercle or mixed vaccine.

Reactions from inoculations of the Non-Virulent T. B.vaccine vary, in some cases there being practically no reaction, while in others there is considerable. For this reason it is advisable to start treatment with a small dose.

When giving a mixed vaccine in conjunction with the Non-Virulent T. B. vaccine, where possible, a bacterial examination should be made to determine the organisms present. This, however, is not always possible because in many cases the infection has not advanced to a point where there is a free discharge of the pus producing organisms. In such cases it is important when selecting a vaccine to associate the mixed infection with the site of tubercle infection. In pulmonary tuberculosis, for example, the organisms usually present in other lung infections will also be found in tubercle infections; in lupus, the usual skin organisms are also present. In pulmonary tuberculosis, the mixed infection most frequently consists of pneumococci, streptococci, staphylococci, and the micrococcus catarrhalis. Tuberculosis of the abdominal viscera and pelvic organs is most frequently associated with colon bacilli, streptococci, pneumococci and staphylococci and would indicate the use of Formula 35. In lupus, staphylococci are the principal complicating invaders and would call for Formula 22. Tubercular joints are complicated by staphylococci and less frequently also by streptococci. This would require Formula 10. The dosage of the mixed vaccine would be the same as when employed in other chronic infections by the same organisms. Treatment is started with the usual small dose and gradually increased.

In the treatment of these cases, it is best to start with the mixed vaccine inoculations, using vaccine Formula 36, 38, 35 or 40, depending upon bacterial findings, the initial dose being 0.2 c.c. This is then followed in 3 to 4 days by the first dose of the Non-Virulent Tubercle Vaccine 100,000,000 organisms 0.2 c.c. of Formula 45 or 0.1 c.c. of 47. The inoculations are then repeated at 3 to 4 day intervals, alternating the

mixed vaccine and the Non-Virulent Tubercle Vaccine, so that the patient receives one dose of each vaccine each week. The mixed vaccine can be increased at each inoculation about 0.1 c.c. until full 1.0 c.c. doses are reached, this being about the maximum dose. The Non-Virulent Tubercle Vaccine can be increased about 100,000,000 organisms per inoculation 0.1 c.c. of Formula 47 until a maximum of 1.5 c.c. is reached. These inoculations are repeated alternately at 3 to 4 day intervals until recovery or the case has been arrested. It is well to continue the vaccine therapy for some months after apparent arresting of the process to prevent relapse and assure permanency of result. Another criterion in dosage is to observe the size of the infiltrated area at the site of inoculation about 18 to 24 hours after administering the vaccine. Having in mind gradually building up these maximum doses, it is well to watch the local reaction and in this way judge the increase, if any, which is to be administered at the particular moment. The local reaction should have an area of infiltration not to exceed approximately 1½ inches in diameter, but it seems necessary to have a little local reaction in order to get the best therapeutic response, particularly in the initial doses. Later a local reaction may not develop, in which case it would be well not to increase the amount at each subsequent inoculation more than approximately 0.1 c.c. even though there is no local reaction. Of course, the focal conditions should be watched carefully after each inoculation, and, if any focal reaction should develop, which is very doubtful, it would be well not to increase the dose until the patient's tolerance permits. The "redness" should practically disappear before administering the next dose. A convenient method of spacing dosage is to give the mixed vaccine, say on Monday and the Non-Virulent Tubercle Vaccine on Thursday or Tuesday and Friday, etc.; in this way the dosage can be regulated conveniently. In some cases where inoculations cannot be conveniently given oftener than once weekly, the mixed vaccine can be given in one location of the body and the tubercle vaccine at another so that the local reaction can be observed independently and the dosage of each be properly increased. Vaccine therapy is not contra-indicated in "temperature cases." It is in these cases that marked results are experienced in bringing down the temperature and eliminating the "night sweats."

Treatment should be continued over a long period of time; at least three or four months, and where the condition has not entirely cleared up, it is necessary to continue the vaccine inoculations for a year or more.

All other measures, such as fresh air, sunlight, rest, plenty of nourishing food, especially raw eggs and milk, should not be neglected. It is the combination of all of these elements that must be utilized to obtain the best results.

THROAT INFECTIONS[1]

THROMBO-PHLEBITIS[2]

TYPHOID FEVER

NO step in advance in preventive medicine has been more spectacular than prophylaxis by means of typhoid vaccine and notwithstanding the positive results obtained it required fifteen years to obtain general recognition. This is another evidence that the medical profession is essentially conservative—too conservative—to render the best service. If typhoid prophylaxis were generally carried out throughout the country the same as in the army, typhoid fever would soon be a rare disease. Since such a measure could only be inaugurated by health authorities, the general practitioner can accomplish much by urging typhoid vaccination wherever possible. This should be particularly insisted upon in communities where typhoid fever prevails and where individuals go on vacation trips. This applies to vacationists and tourists generally either during the summer in the north or during the winter in the south.

A few years ago much was said concerning the advantage of giving a single dose of lipo-vaccine, but the use of this vaccine in the army service has shown that the reactions often are unnecessarily severe. These severe reactions are avoided by the saline suspension. Three doses at 7 to 10 day intervals are necessary. The first dose should be 0.5 c.c. of Formula 46 or 30 and the two subsequent doses 1 c.c. each.

From our experience we contend that no case of typhoid fever is efficiently treated without the use of a vaccine and the earlier the vaccine is given the better the results. No depressing effects or negative phase from the use of a vaccine in typhoid fever has ever been reported. The experienced practitioner, especially when typhoid fever prevails, usually recognizes the clinical symptoms early. A positive Widal appears too late to be relied on as a positive diagnosis before instituting vaccine treatment. A blood culture to determine the presence of typhoid bacilli will furnish an earlier positive diagnosis. Ordinarily the characteristic clinical symptoms will suffice. If vaccine treatment is started during the first few days of fever, a normal temperature may be expected by the twelfth or fifteenth day. A positive Widal seldom appears before the eighth day of fever. If vaccine treatment is then started, the patient is usually sufficiently toxic to retard rapid immunization with vaccine.

Treatment should be started by giving about 250,000,000 or 0.3 c.c. of Formula 46 or 30 and repeated at 1 to 3 day intervals, increasing the dose by 0.1 or 0.2 c.c. each time until the temperature becomes about normal, then treatments should be extended to 4 or 5 day intervals and continued until convalescence is complete.

[1] See Tonsillitis and Rhinitis. [2] See Phlebitis.

The first indications of improvement are seen in a subsidence of nervous symptoms and a decidedly brighter appearance of the patient.

Complications may arise from mixed infections when mixed vaccines in conjunction with typhoid vaccine are indicated. Pneumococci, streptococci, staphylococci are present if broncho-pneumonia develops, and in severe bowel complications these same organisms with the colon bacillus are primary complicating factors. So if such complications develop, Formula 35 should be administered in conjunction with the typhoid Formula 30 or 46.

George H. Weaver, speaking of the early treatment of typhoid fever with typhoid vaccine, reports that:

"When the treatment was commenced within the first week, the mean duration of the febrile period was sixteen days; when it was commenced in the second week, the mean duration was twenty-one days; when it was commenced in the third week, the mean duration was twenty-three days. These figures show that vaccine therapy can shorten the febrile period."

URETHRITIS[1]

URINARY INFECTIONS[2]

URTICARIA

THIS obscure skin affliction is often due to eating certain kinds of protein to which the person is sensitized. If it can be determined which protein is responsible for the condition, the patient may be desensitized by the hypodermic injection of preparations made from such a protein.

Very often the cause of urticaria is very obscure but in such cases relief is often obtained by the hypodermic injection of a mixed vaccine. Formula 35 serves the best purpose. Here the results are probably obtained from the nonspecific immunizing influence of the vaccine which causes the desensitization from whatever source it may be caused. The vaccine is given in the usual dosage employed in the treatment of chronic infections.

VARICOSE ULCERS

IN the treatment of Varicose Ulcers, we have two essential conditions to deal with. Congestion, due to impaired circulation, and infection. Both of these factors must be dealt with to obtain the best results. To relieve the congestion, rest in bed with the leg elevated answers the best purpose, but many such people cannot afford the time to remain in bed. A suitable elastic bandage applied on rising and worn all day will do much toward relieving this congestion and will aid materially in the healing process.

[1]See Gonorrhea.
[2]See Cystitis, Nephritis, Gonorrhea.

The usual skin cocci are commonly present and somehow the colon bacillus is also often found. Formula 35 will aid very materially in procuring healthy granulation so skin growth becomes possible and in cases of extensive ulcers, skin grafts will take and grow. The vaccine is given in the usual dosage employed in the treatment of chronic infections and should be continued for several months at weekly intervals after the ulcer is healed to guard against relapses.

VULVITIS[1]

VULVO-VAGINITIS[1]

VERTIGO

THIS disagreeable ailment has been definitely traced to an inflammatory process due to chronic infection of the internal ear apparatus, more particularly the semicircular canals or the nerves leading thereto. The semicircular canals are known to be the organs of equilibrium. If these canals are irritated on either side, a disturbance of equilibrium takes place at once with a resulting dizziness. That this inflammatory condition is due to infection is evident from the fact that these cases follow nonsuppurative inflammation of the middle ear; due to pus accumulation of the middle ear, aural suppuration and involvement of the nerve trunk.

Another evidence that aural vertigo is due to infection leading to the internal ear apparatus or the semicircular canals themselves is the results obtained from therapeutic immunization. We have treated twenty-nine successive cases with bacterial vaccines, and, as far as we have been able to follow them, all have remained well. In many cases marked improvement is observed after the first inoculation while in others treatment must be continued for some months before much benefit is obtained. This vertigo is often associated with tinnitus aurium, and while we have never seen the tinnitus improved, the vertigo has been cured. It has been observed that this vertigo is more severe during high blood pressure. This may be explained thus: Under high blood pressure the inflamed area would become more sensitive with a resulting increased vertigo.

The streptococcus is the most frequent primary infective agent in middle ear inflammations and with its tendency to invade surrounding tissues is most likely to involve the internal ear also. So streptococcus vaccine is logically employed. A combined vaccine, however, that contains the organisms usually responsible for otitis media (Formula 6 or 40) probably serves a better purpose. Treatment is started with the usual dose employed in chronic infections 0.2 c.c. and gradually increased to 1 c.c., making inoculations at 5 to 7 day intervals.

1 See Gonorrhea in Women.

WOUND INFECTIONS

ABRASIONS of the skin from slight cuts, scratches, needle pricks, tramping on a nail, etc., are a few of such common occurrences that as a rule they are disregarded and heal over without any special treatment, but often these trivial injuries become infected with virulent pathogenic organisms and a physician is only consulted after the infection has extended beyond the reach of local antiseptic treatment. In cases of more extensive injuries, a physician is usually called to take care of the fresh wound, but even in such cases the most vigilant efforts of the doctor will fail to cleanse the wound sufficiently to avoid infection. Wounds are often penetrating or lacerated to such an extent that cleansing to an aseptic condition is impossible.

When treating wound infections, a possible tetanus infection must always be carefully considered. The character of the wound and the circumstances surrounding the receipt of the injury may throw much light on this subject. A superficial wound that has not been tightly bandaged is not liable to contain tetanus bacillus, because the germ being anaërobic will not grow when exposed to the air. The tetanus bacillus is prevalent in rich soil or barn manure and injuries exposed to such filth should always be regarded as being in danger of tetanus infection. Penetrating wounds like those caused by toy pistols in the dirty hands of the average boy are always liable to tetanus infection. The injury, as a rule, is small and if disregarded may lead to serious consequences. Whenever there is the slightest suspicion that a tetanus infection may be present, an immunizing treatment of antitetanic serum should be given at once. Antitetanic serum has proven its value as a prophylactic agent while its curative value after symptoms of tetanus have developed is not so well established.

After excluding a possible tetanus infection, the streptococcus must be regarded as the most probable dangerous infecting organism. Infections by this organism are usually quite characteristic. Streptococcus infections have a distinct tendency to spread rapidly and in the early stages of the infection usually run along lymphatic channels, leaving red streaks extending from the site of infection. Staphylococcus infections of wounds are common, but as a rule, infections by this organism remain confined to the area immediately surrounding the infected wound. Occasionally, however, staphylococcus infections assume dangerous proportions. Microscopic examination of slides prepared from the pus procured from these wounds will throw much light on the character of the infection and where possible cultures should be made to determine the character of the infection; but in no case should vaccine treatment be withheld until a positive diagnosis by bacterial examination is made. Clinical symptoms are usually sufficiently characteristic so a vaccine can

be given on a clinical diagnosis and by this means secure the advantages which early treatment offers. Since staphylococci are common complicating factors in streptococcus infections, strepto-staphylococcus combined vaccine (Formula 10) should be given at once and inoculations repeated at 1 or 2 day intervals until the inflammatory symptoms subside. After that, the vaccine should be given at 3 or 4 day intervals until the infection has entirely subsided. If bacterial examination should show some unusual organisms present, a vaccine corresponding to the organisms found should be given or an autogenous vaccine employed.

The results from early vaccine treatment in wound infections are striking. Generally the inflammatory symptoms will subside within twenty-four to thirty-six hours after the first inoculation. If the vaccine is given after the infection has taken on extensive proportions, such striking results are not observed, but if the vaccine inoculations are persistently carried out even such cases often improve rapidly.

WHOOPING COUGH

THE efficiency of whooping cough vaccine in the treatment and prevention of whooping cough is now generally recognized.

The great danger from whooping cough is due to the possible development of broncho-pneumonia. That this broncho-pneumonia is due to a mixed infection in which the pneumococcus, streptococcus and staphylococcus are prominent factors in conjunction with the Bordet bacillus is well established. Furthermore, much of the bronchial disturbance during the ordinary run of the disease is due to the same organisms. Disregard of this fact has been responsible for many of the failures in attempting therapeutic immunization in whooping cough. Efficient therapeutic immunization demands an immunizing agent that contains the entire variety of pathogenic organisms involved in the infective process. To give a straight Bordet bacillus vaccine in an advanced case of whooping cough with extensive mixed infection is inefficient treatment. Furthermore, after the infection is once well established, we never can know whether a mixed infection will develop, even if not present. For this reason, since prevention is better than cure, it is advisable to employ a mixed vaccine containing in conjunction with the Bordet bacillus the other organisms commonly found in cases of whooping cough which is advantageously combined in Formula 43.

Treatment should be started early by giving 0.3 c.c., and, if no material reaction follows, the dose should be increased to 1.0 c.c. within three or four treatments, making inoculations at 3 day intervals. In extremely severe cases, it is of advantage to work up the dose to 2.0 c.c. In some cases, not much improvement will be observed during the first or second week, while in many cases marked improvement will take place after the

first injection. Almost invariably at the end of the third week the cough will subside even in extremely bad cases. After the cough subsides, treatment should be continued for a month or more by giving the vaccine at weekly intervals. If this is not done, the cough is liable to return. In cases that have developed broncho-pneumonia, it is necessary to push the treatment more vigorously by giving the vaccine at daily intervals and in extremely bad cases with high temperature, it is best to give the vaccine at 12 hour intervals. Extremely acute cases also require large doses, from .5 c.c. to 1.0 c.c.

The prophylactic value of whooping cough vaccine is also well established. This prophylaxis is best accomplished by giving a straight polyvalent Bordet bacillus vaccine (Formula 37). The first dose should be 0.5 c.c. and then two or three subsequent doses of 1.0 c.c. should be given at 3 to 5 day intervals. Reactions from this vaccine are moderate and cause little or no disturbance.

Giving vaccines to infants and small children is most readily accomplished by having the little patient lie across the nurse's lap with the buttocks exposed. While the nurse holds the legs with the right hand and the arms with the left, injection may be made, without any inconvenience, into the subcutaneous tissues of the buttocks.

Appendix

VACCINATION IS 2,000 YEARS OLD

"VACCINATION is an outgrowth of man's effort to protect himself from pestilence by using nature's methods of defense," says Dr. G. W. McCoy, director of the Hygienic Laboratory of the U. S. Public Health Service. "Primitive man noticed that recovery from a first attack by most diseases gave immunity against other attacks; and, some 2,000 years ago, he began to inoculate his fellows with smallpox when conditions seemed propitious instead of waiting for nature to do it at some time when conditions might be very unpropitious.

"Inoculations against smallpox were made in India and in China as early as 300 B. C. Later, when the disease reached Europe, inoculation went with it, supplemented by a new method called 'selling smallpox'—exposing a well person to contact with one ill with the disease so that, if he survived, he would be proof against it.

"Inoculation differs somewhat from vaccination as devised by Jenner, but the principle is the same. Moreover, long before Jenner's day, it was known that an attack of cowpox gave immunity from smallpox; and records show that men who had recovered from cowpox had themselves inoculated with smallpox to make the proof conclusive. Jenner, however, as he himself says, 'placed vaccination on a rock' where he knew it would be immovable.

"Before the days of vaccination, conservative estimates show that one-third of all persons had smallpox and one-tenth of all deaths were due to it. Today, smallpox is rare. Many physicians have never seen a case; and where vaccination is consistently practiced, no deaths from it occur. Formerly, smallpox was considered a children's disease; and it still is a child's disease—where infantile and school vaccination is neglected. Witness the Philippines, where, four or five years ago, after years of neglect of vaccination, an epidemic swept away nearly 50,000 persons, a large percentage of whom were children under ten years of age.

"In the United States, well-vaccinated communities show low smallpox rates—Maryland with 0.1 case per thousand population; New York with 0.025 per thousand, and the District of Columbia with 0.14 per thousand. Poorly-vaccinated states tell another story: Oregon with 1.45; Washington with 1.72; and Kansas with 2.0 per thousand population.

"Some communities wait till an epidemic breaks out and then rush to vaccinate. This stops the disease—after it has caused many deaths and has 'branded' many survivors. Sixteen months ago, in Kansas City, an

epidemic of smallpox began, yielding 350 cases and 123 deaths; and a few months later another started in Denver and yielded 950 cases and 288 deaths. Such epidemics always eradicate the opposition to vaccination in the community—for a time."—*The American Journal of Clinical Medicine*, July, 1923.

THE SCOPE OF VACCINE THERAPY[1]

By C. E. Jenkins, M. R. C. S. Eng.,
Pathologist, Salford Royal Hospital

THE utility and limitations of vaccine therapy are questions which resolve themselves into a consideration of two interdependent factors—the patient and the vaccine. It will be convenient to discuss them together. All cases which can be treated by vaccines are divisible into three main groups; the division is of more importance than mere academic classification, for the success of the treatment will often depend upon the discrimination of the clinician or the bacteriologist in allotting a case to its correct group. The first group comprises the cases in which cure or alleviation of a disease actually present is desired. To the second group belong that large mass of healthy people who require a vaccine for prophylactic purposes—that is to say, to acquire protection against some disease which may attack them at a future date. The third group is the one which causes confusion. To it belong the cases which require prophylaxis primarily, but which at the same time are in need of cure.

The Suitable Cases

Group 1.—It is a commonplace that the two cardinal requirements of a successful vaccine are that the disease it is proposed to treat shall be a bacterial disease, and that the vaccine shall be prepared from the causal organism. Even so, success cannot be guaranteed. Other subsidiary factors, although separately of small moment, exert collectively a very important influence upon the final result. First, the patient's condition must be capable of improvement, for no vaccine can repair, or rather recreate, a tissue already completely destroyed. Thus a vaccine will frequently benefit a case of long-standing chronic bronchitis to the extent of abolishing the dyspnœa, asthmatic attacks, cough, and that anæmia which frequently accompanies the condition. But it cannot be expected to cure the emphysema, the presence of which is a standing and irremovable threat of future trouble if the patient becomes too confident of his powers of resistance and therefore careless. It is hardly necessary to observe that such factors as age, opportunity of rest, and undermining of resistance by long toxic absorption all count in the ultimate result. Alco-

[1] An abstract of a post-graduate lecture delivered at the Salford Royal Hospital.

holic excess is a well-known predisposing cause of bacterial invasion, both acute and chronic, but it has often to be pointed out to the patient that whilst the vaccine may cure his present illness it is unlikely to confer upon him what he would regard as the high privilege of a permanent and absolute immunity from all the unpleasant effects of strong drink.

Another type of case often benefited by vaccine therapy comprises those sufferers from a disease in which one sets out frankly to treat a secondary infection or a complication, leaving the primary cause to the patient to deal with as best he may. Such conditions as the valvular lesions of the heart complicated by chronic bacterial pulmonary infection are of this nature. The fact that in most cases the cardiac lesion had a bacterial origin is beside the point. The damage has been done, the causal organism has disappeared, and all one can do is to mitigate the damage. Pulmonary tuberculosis or what is called the "open" type is another example. Here the primary disease is complicated by secondary infection by the common parasitic organisms of the respiratory tract, and the patient's chance of recovery is not rendered any easier thereby. If the secondary sepsis can be removed, a better opportunity is afforded for fibrous healing to occur.

The isolation of the causal organism may be simple or a matter of much difficulty, such difficulty lying in the identification of causation rather than in the trouble to obtain a growth of the suspected organism in a culture. The intestinal tract furnishes the most conspicuous example. There are many toxic conditions which are due to the fæcal streptococcus, and a culture of the fæces occasionally yields a growth which puts the question beyond doubt. An instance was a profound toxæmia accompanied by an erythematous eruption and liquid stools of appallingly offensive odor. A culture yielded a mixed growth of the streptococcus and a diphtheroid bacillus, with complete absence of the colon bacillus. A vaccine produced a complete recovery. But the majority of the cases are not so simple. It is usual to find the streptococcus and the colon bacillus present, and the problem to be solved is to decide whether either of them can be fairly described as being present in abnormal numbers or as having unusual characters. An example of the latter was a purulent colitis of unknown origin in which two distinct types of colon bacillus were recovered. A vaccine made from the aberrant form was highly successful. It is obvious that each and every case must be decided upon its merits, and the bacteriologist must guard himself well against an imagining of vain things.

Group 2.—The conditions that govern the composition and use of prophylactic vaccines are of a simple order. It is required to protect a patient from the risk of contracting any disease or group of diseases at some future date. It is, therefore, essential that the vaccine shall contain all organisms likely to cause infection, and in stating this requirement one

may draw attention to the importance of using in the vaccine several strains of each of the organisms. The duration of the immunity so conferred is variable, but twelve months is the minimum for most organisms. The subject of immunity is one which the patient should have explained to him. All immunity is only relative, and whilst it is probable in a given case that the inoculated person will be absolutely free from attack, yet it is by no means certain, and the patient should realize that such is the case. On the other hand, it may be promised with some certainty that any attack that may occur will be mild in type and of short duration.

Group 3.—Much the commonest clinical condition belonging to this group is recurring catarrh of the respiratory passages. The type of case which requires vaccine treatment for catarrh is large in numbers and shows much variety in the clinical nature of the most prominent symptoms. The typical case complains of a nasal catarrh or a bronchitis that varies greatly in intensity with the weather and the season: occasionally he is quite free from it, but the slightest exposure brings it back as an acute attack to be followed by weeks or months of chronic rhinitis or bronchitis, the latter being commonly associated with asthma. The constant drain upon the patient's resistance gradually brings about a general lowering of his health, vigor, and capacity for work.

The question of a vaccine is usually considered when the patient has reached this stage, and he generally presents himself for examination by a bacteriologist shortly after an acute attack. A copious nasal discharge or sputum is still present and seems to invite forthwith a culture and an autogenous vaccine. It is a mistaken policy. A purely autogenous vaccine is the correct type to employ as a curative measure for the infection then existing, but if it is expected to exercise a prophylactic power against future attacks it implies that one expects all subsequent infection to be due to the same organism, and that the patient has a special susceptibility where that organism is concerned. A very little experience will suffice to demonstrate that, except in a few rare instances, this is not so. The patient's weakness does not lie with a solitary organism; it is a general lack of resistance on the part of his respiratory tract against bacterial infection in general. Therefore, a vaccine should be designed to cover all the organisms commonly encountered as infective agents of the tract, and since it is desirable to combat the immediate infection as well, a semi-autogenous vaccine, composed of the organisms recovered at the moment and combined with a good multi-strain stock vaccine of the other organisms, is the vaccine most likely on theoretical grounds to give the best results. Practical experience has convinced me that the theory is sound.

This method of preparing a vaccine is particularly useful in the treatment of chronic rheumatism and rheumatoid arthritis, where the preparation of a vaccine is always somewhat empirical in spite of such discoveries

as a gratifying purity of streptococcal growth obtained from a pocket of pyorrhœa. The proportions in which a semi-autogenous vaccine is compounded afford scope for individual preference on the part of the bacteriologist, but three-fifths of the autogenous organisms with two-fifths of the stock will be found very generally useful.

Dosage

The dosage of vaccines is still a controversial subject. It may be considered with reference to three points—the amount of the dose, the intervals between doses, and the total number given. It is neither desirable nor necessary to produce a really serious constitutional disturbance. The therapeutic result will be no better at the end of the course, whilst an initial general reaction of considerable unpleasantness may make the patient disinclined for any further injections. These considerations, therefore, impel one to conclude that it is sound policy to give doses which produce at most nothing more than a few hours' "tired feeling" after each of them. The intervals between the doses should be from 5 to 7 days. A clinical improvement is often seen in a shorter time, but the patient is hypersensitive for three or four days after each injection, and may develop a profound reaction if the interval is made as short as two days. The number of injections should not exceed eight. Prolonged courses frequently produce a state in which the patient fails to react to any dose. The final degree of improvement shows itself about three weeks to a month after administration has ceased. If a second course is deemed desirable later, an interval of four or five months should elapse before commencing it. There are many types of vaccines, but only two need notice. The first is the old simple vaccine, most used at present; the other is the residual, or detoxicated, vaccine, which is challenging the supremacy of the first-named. The residual vaccine has many practical advantages, and I have yet to see a case in which the old type is preferable, or even equal, to the residual vaccine in the improvement it produces.

The Relationship of Vaccine Therapy to Other Forms of Treatment

As a general rule, a vaccine is a last resort, only invoked when other means have failed or offer no reasonable prospect of benefit. But the fact that these other remedies are in themselves not sufficient should not cause them to be abandoned when vaccine treatment is started. Each reinforces the other and contributes to the only result that matters—cure. This combined treatment is seen at its best in acute and chronic gonorrhœa. The residual vaccine is the best single remedy, but it would be folly not to assist it with the older remedies appropriate to the condition.

Lastly, vaccines are being used today with increasing frequency as preparatory remedies for increasing the prospect of success in operative

work where urgency is not indicated. At present this field of usefulness is almost confined to the surgery of the nose and throat, but the field might well be widened. It is scarcely necessary to add that the cases in this field belong to the third group, and that the most suitable vaccine to use is the semi-autogenous.—*The Lancet*—Sept. 9, 1922.

ACUTE PNEUMONIA AND INFLUENZA BRONCHO-PNEUMONIA

Delivered at the General Hospital, Birmingham

By W. H. Wynn, M. Sc. Birm., M. D., F. R. C. P. Lond.

Hon. Physician to the General Hospital, Birmingham

PNEUMONIA ranks first of all acute diseases as a cause of death in civilized countries. Its death-rate now exceeds that from pulmonary tuberculosis. It is no respecter of persons, attacking both the weak and the strong, and although Osler called it the friend of the aged, who through its aid escape the "cold gradations of decay," more persons die from it between thirty-five and fifty-five than at any other period. No disease is so great a foe to the hard-working business or professional man, who is not seldom taken off by it before he reaches the years of leisure.

We can appropriately consider the treatment of influenzal broncho-pneumonia with that of acute lobar pneumonia, as the broad principles are the same, though there is some difference in details. The usual method of treatment of these diseases has been called expectant, and this should aim at placing the patient in the best environment for his fight and prescribing those measures which will support him until he succeeds or fails in his venture. Such expectant treatment has certainly succeeded better than the active bleeding and purging of an earlier period, but faced with a mortality of twenty per cent. in lobar pneumonia and thirty per cent. or more in influenzal broncho-pneumonia we must acknowledge that we are incompletely equipped and need new weapons. There has, in fact, apart from specific therapy and improvements in nursing, been no real advance in our treatment since the eighteenth century. In contemporary accounts of an epidemic of influenza in 1782, we find the same discussions concerning the use of Peruvian bark, expectorants, diaphoretics, and opiates as still rage around their modern representatives. Much of our present treatment is merely traditional and without rational basis.

Until some drug is discovered which, in therapeutic doses, will destroy the pneumococcus within the living body recovery from pneumonia can only take place by the patient providing antibodies to overcome the bacteria and their toxins. It is to specific therapy that we must, therefore, look for aid, and I think that we do not look in vain. Without waiting for serum treatment to become practicable, I am convinced that we have

in vaccines a means, when used promptly and decisively, of aborting the disease and lowering its mortality. I first treated pneumonia and other acute diseases with vaccines in 1907, and the method which was evolved and was published in the *British Medical Journal*, March 13th, 1915, has borne the test of time and proved equally successful in its application to influenzal broncho-pneumonia during the recent epidemics.

Early Diagnosis

Vaccines, as with other methods of specific treatment, must be used as early as possible. They can give little or no assistance when the infection has been allowed to go on to the point of cardiac and nervous exhaustion. Their object is to control the infection before it gets out of hand, and they should not be used as a last resort in cases which are not doing well under other treatment. When given within the first twenty-four hours after the onset of fever, brilliant results are obtained, but with each hour that passes success is less certain. In this we have an exact parallel with the antitoxin treatment of diphtheria. Pneumonia, influenza, and other acute infections must be regarded as acute medical emergencies demanding prompt action, in the same way that a perforated duodenal ulcer and acute appendicitis are regarded as acute surgical emergencies. The abandonment of expectant treatment in surgery has led to a great saving of life. Few physicians have seen many cases of pneumonia within twenty-four hours of its onset, but when they can offer as definite assistance as the surgeon, they will be called into consultation at a stage when such assistance will avail. Prompt action requires prompt diagnosis. Too often the diagnosis of pneumonia is not made until consolidation of the lung is present. One is commonly told, "This man has been ill for three days with a high temperature, but it was only today that he showed signs of pneumonia," as though previously he had been suffering from some other disease. It is also implied that consolidation is a bad thing and that the patient had taken a turn for the worse. This confusion of the disease with one of its pathological manifestations is a great hindrance to early diagnosis. The early symptoms of acute pneumonia are so striking that diagnosis should be possible within a few hours. The initial rigor, the rapid rise of temperature, hot dry skin, the pain in the side, the grunting shallow respirations make up a picture not seen in any other disease. Alterations in breath sounds can be found within a few hours, and I have seen blood-stained sputum within three hours of the onset of fever. With influenzal broncho-pneumonia, the picture is not so characteristic, but, although complications may gradually develop in the course of a severe simple influenza, it is more usual for them either to be present from the beginning or after a few days of mild fever there is a rapid rise of temperature and the case takes on a graver aspect. In

either disease, it should be possible to take prompt measures within twenty-four, or at most forty-eight, hours of the onset. We are given a margin of time in which the issue of life and death are in our hands. If we allow this opportunity to pass, the issue, in so far as it depends upon a conflict with the invading organisms, is mainly beyond our control.

Preliminary and General Treatment

Whatever treatment be adopted, certain preliminary measures are fundamental. The patient's fate is mainly decided within the first two days. Much can be done to prevent the onset of symptoms which later we should be helpless to combat. Precise and detailed instructions must be given, especially as most patients are nursed by unskilled relatives. Before all things, I would place absolute rest and free ventilation. From the first, patients must be kept strictly in bed. Most patients object to use a bed-pan and, unless strict orders are given, it will be found that they continue to get out of bed as long as it is physically possible. Nurses and even doctors do not always appreciate the need for absolute rest. Too much effort is often caused by routine washings and scrubbings, reaching out for the sputum mug and feeding cup, sitting up to cough, etc. When rolling a patient gently over to examine the back, one is not seldom told, "Oh, he can sit up all right, he always does so for me!" One garment should be worn and much exertion is saved by slitting this down the middle, and so preventing an agonising struggle to get nightshirt and vest over the arms and head.

Windows should be widely open night and day and the bed unscreened in the center of the room. The temperature of the room should not exceed 60°, and the atmosphere should feel fresh, with air in constant movement. Fresh air is the finest circulatory tonic we possess. But with our care to avoid the close, stuffy, over-heated room, we must not go to the other extreme and expose patients to icy draughts of cold air. During the initial stage and also at the crisis, the patient will feel chilly and abundant bedclothes are required, but when the fever is established, one sheet and blanket are sufficient. Gamgee jackets are in fashion, and a nurse will probably put one on unless definitely told not to. I fail to see the necessity for wrapping a patient whom we desire to lose heat in cotton-wool. Patients and their friends still think that pneumonia is caused by exposure to cold, and should be therefore treated by heat. Sleep will be promoted and restlessness allayed by attention to these common-sense details.

A useful routine diet of milk (citrated if there is vomiting) and albumin water, 5 oz. of each alternately every two hours. Some of the feeds of milk can be flavored with tea or coffee, or malted milk given instead, and sugar should be added, especially in the form of cane or milk sugar. Water

or lemon-water up to four or five pints in the twenty-four hours, but in small quantities at a time, should be insisted upon. Unless definitely ordered, patients seldom get enough, and one is constantly told by the friends, "We did not like to give him cold water, although he has been craving for it, as we thought it dangerous." The laity still have much faith in beef-tea, especially in one well-advertised and expensive brand which contains three parts of coagulable protein in 1000. For the sake of the flavor, a little may be added to the albumin water, but otherwise, it should have no place in the sickroom.

The hygiene of the mouth requires constant attention. Dentures should be removed. The mouth should be wiped out every two hours, and if necessary more often, with a rag moistened with a diluted watery antiseptic. Glycerine should be avoided because of its hygroscopic property. A liquid paraffin spray to the nose helps the patient's comfort. Three grains of calomel at the onset, followed by a saline, can be given. Thereafter, if skilled nursing is available, a morning soap-and-water enema can be given, if necessary for constipation, or failing that, a dose of sodium sulphate. No drug at present known will control the infection, but a mild diuretic, such as pot. citrat. gr. 30, liq. ammon. acetat. dr. 4 aq. camph. oz. 1, four-hourly, is helpful.

Vaccine Treatment

I know nothing in the whole range of medical treatment so dramatic as the rapid defervescence which follows the injection of a suitable dose of vaccine to a patient suffering from pneumonia or influenzal pneumonia within twenty-four hours of its onset. The vaccine I have used is made from primary cultures or at most first subcultures. It should not be detoxicated, or sensitised. For acute pneumonia the vaccine contains several strains of pneumococci, and for influenzal broncho-pneumonia equal numbers of pneumococci, streptococci, and influenza bacilli. Various formulæ have been devised for this triple vaccine containing different proportions of the three organisms. I know no good reason for this, and have obtained the best results with a vaccine containing equal numbers of each. The important points are that it should be given early and in sufficient amount. In pneumonia, I give 100 millions pneumococci to an adult and in influenzal broncho-pneumonia 100 millions of each organism. For a child of twelve to fourteen, 40 to 50 millions should be given, and to a child of two or three, 10 to 20 millions. These doses have been arrived at after many years' experience, during the earlier part of which smaller doses were used and were found to be ineffective. I have seen much larger doses used with safety as I shall discuss later. When such a dose is used during the first day of the disease in the majority of cases the temperature falls to normal on the following day and no further treatment is

required. With each day's delay such rapid defervescence becomes less likely and the dose may have to be repeated. This can be done every twenty-four hours until the temperature has fallen. When injection is delayed until the fourth day or later, little can be expected from specific therapy. Toxins will then have already damaged heart muscle and nerve cells. The object of vaccine treatment is to prevent this damage; it can have no action upon heart failure or nerve exhaustion.

The earliest case of pneumonia I have treated was a man of 40 who at 8 p. m. one evening was working in his garden, apparently quite well. One hour later he had a violent rigor and sent for his doctor who arrived at 11 p. m. His temperature was then 104° F. and respirations 36, he had pleuritic pain and grunting respiration. When I saw him in consultation just after midnight he already had blood-stained sputum. His temperature was then 105°, respirations 38, and pulse 128. I injected 100 millions pneumococci. This was followed by a fall of temperature, which reached normal at 4 p. m. the following afternoon, about nineteen hours from his first symptom. For a few days afterwards he had consolidation of two lobes, with complete absence of symptoms. Another early case was that of a doctor aged 53, whom I saw one evening about 12 hours after the onset of shivering. His temperature was then 105°, respirations 36, and pulse 136. There was impaired resonance, with altered breath-sounds and fine crepitations at the base of his right lung. A dose of 100 millions pneumococcic vaccine was followed by a fall of temperature, and when I saw him at 10 a. m. next morning his temperature was normal and the pulse-rate only 68. Again there was the striking phenomenon of a patient with consolidation of a portion of the lung and an absence of symptoms. Many similar cases could be quoted. Of those inoculated during the first day the temperature became normal in twenty-four hours in 83 per cent and within forty-eight hours in 100 per cent. Of cases injected during the second day 57 per cent had a normal temperature in twenty-four hours, 71 per cent in forty-eight hours, and 93 per cent in three days. But of those injected on the third day only 20 per cent were normal in twenty-four hours, 60 per cent within forty-eight hours, and 73 per cent within three days. In a series of 100 consecutive cases injected for the first time at various stages the following were the results. On the first day, 10 cases with one death. This was in a lady aged twenty-nine who was pregnant at full term and hourly expecting her confinement. She was injected within twenty-four hours and the temperature fell to 98.4° in six hours. Labor occurred the following day with much difficulty. She had consolidation of nearly the whole of the left lung and a patch at the base of the right lung. For a time the outlook seemed hopeful, but she died from heart failure on the sixth day. This is the only fatal case out of a large number injected

during the first or second day. On the second day, seventeen cases, no deaths. On the third day, twenty-two cases with no deaths. On the fourth day, sixteen cases with three deaths (1 a baby of 12 months, who had always been feeble, and another an adynamic case in a patient of 65). On the fifth day, nine cases with three deaths. On the sixth day, seven cases with two deaths. On the seventh day, five cases with one death. On the eighth, four cases with no deaths; and on the ninth, one case with no deaths. Nine cases had an uncertain date of onset, but were injected late, and three died. Out of forty-nine cases injected within three days only one died, and this was complicated by labor; the remaining twelve deaths occurred in patients injected on the fourth day or later. All these were cases of severe pneumonia, such as are seen in hospital and consulting practice. They do not include the milder cases, so often seen in general practice, which give rise to no anxiety.

It was a natural step from the vaccine treatment of acute pneumonia to that of influenzal broncho-pneumonia. Whatever be the true nature of the primary infection in influenza, there is agreement that the serious pulmonary complications are associated with the presence of streptococci, especially of the hæmolytic variety, and pneumococci, and that the influenza bacillus is commonly if not invariably present. Experience had previously shown that broncho-pneumonia of other origin would also yield to vaccine treatment. Influenzal broncho-pneumonia during an epidemic period, however, resembles lobar pneumonia in that an active stock vaccine can be prepared for immediate use, whereas with other broncho-pneumonias some time is lost in discovering the nature of the infection.

The result of vaccine treatment of influenzal broncho-pneumonia can be illustrated by the records of 107 hospital patients injected during the first five days of their illness. These patients suffered from the severe type of the disease, and the term broncho-pneumonia is used to include a variety of pulmonary lesions—bronchiolitis, extreme congestion, collapse, œdema, pleurisy, and consolidation. Many had severe confluent broncho-pneumonia and others would be more rightly classified as influenzo-pneumococcic or streptococcic septicæmia. Several were admitted in a seemingly hopeless condition, and many had the characteristic heliotrope cyanosis. Of the one hundred seven cases, twenty-eight were injected on the first day of their illness, twenty-three on the second day, twenty-two on the third, twenty on the fourth, and fourteen on the fifth. I give the results in tabular form:—

Day of first injection	Cases	Recovered	Died	Temperature normal in—	
				24 hours	48 hours
				Per cent	Per cent
1st	28	28	0	71.4	85.7
2nd	23	22	1	47.8	56.5
3rd	22	20	2	50.0	72.7
4th	20	15	5	30.0	40.0
5th	14	12	2	35.7	63.5
—	107	97	10	50.0	65.0

The only death of fifty-one patients injected within the first two days of their illness occurred in a young woman of 29, who was admitted on the second day with violent mania and extensive broncho-pneumonia. She shouted and struggled incessantly. The first injection of vaccine was followed by a fall of temperature to normal in thirty-six hours, and the patient became more rational, but she died unexpectedly on the ninth day from pulmonary embolism. Seven out of the ten deaths occurred in patients who were not injected until the fourth or fifth day. Four were complicated respectively by mitral stenosis, advanced pregnancy, meningitis, and asthma, and three others had considerable albuminuria. The ten deaths give a rate of 9.1 per cent.

Analysis of the results emphasizes the importance of early treatment. Whilst 71.4 per cent injected on the first day had a normal temperature within the following twenty-four hours and in some there was complete defervescence in twelve hours, on the second day the percentage had fallen to 47.8, on the third day to 50, on the fourth day to 30, and on the fifth day to 35.7. Of the total one hundred seven cases, the temperature fell to normal within twenty-four hours in 50 per cent. The youngest patient, a baby of three months, was admitted with a temperature of 104.2°, respirations 60, and a pulse of 160 or more. Two doses of 7½ millions vaccine were given with complete recovery. Another baby of nine months, with a temperature of 104°, respirations 60, and pulse 164, was injected on the fourth day with 10 millions and the temperature fell to 99° in less than twenty-four hours. The oldest patient, a man of 73, was given 60 millions on the first day and the disease was aborted.

These effects of early vaccine treatment in aborting the disease are not peculiar to pneumonia. They can be seen with cerebro-spinal fever, typhoid fever, and streptococcic septicæmia, when early diagnosis is possible. We appear to be dealing with a general principle capable of wider application when we more thoroughly understand the mechanism of immunity.

The chief obstacle to the general use of vaccines in acute disease has been the fear of producing a negative phase. Hence when vaccines are used it is too often in ineffective doses. The theory of the negative phase

was evolved from the study of cases of chronic localized infections. Under such conditions the patient is "sensitised" and the injection of a small dose of vaccine may have a profound result. But in pneumonia the patient is not in the same state of sensitisation, and after quite large doses of vaccine there is no evidence of a negative phase. Although I have found 100 millions to be a sufficient dose when an active vaccine is used, I have seen much larger doses given. Recently, I saw in consultation a stout middle-aged man who, after four days' mild influenza, developed broncho-pneumonia with a temperature of 104.5°. His doctor injected him by mistake with 1 c.cm. of the mixed anti-influenza vaccine (St. Mary's Hospital formula) containing 1,000 millions pneumococci, 500 millions B. influenzæ, and 100 millions streptococci, the full dose for prophylaxis. I saw the patient eleven hours later; his temperature was 101°, he had lost his distress, and was distinctly better. He had a good night and next morning had a normal temperature. This unintentional experiment, I think, supports my contention that there is no clinical evidence of a negative phase after injection of quite large doses of vaccine during the early stages of pneumonia. In typhoid fever the same fact is seen, for whereas the usual initial dose is 250-300 millions, some authorities give as much as 1,000 millions increasing to 2,000 millions of an ordinary, not detoxicated or sensitised, vaccine.

Those unfamiliar with vaccine treatment are apt to think that whilst large doses can safely be given to patients with chronic disease, acute infections must be treated with very small doses. But the contrary is the fact; the treatment of chronic infections should be cautiously commenced with quite small doses. It is easy to produce severe reactions with small doses in patients suffering from chronic bronchitis, asthma, arthritis, pyelitis, chronic septicæmias, and similar conditions, in all of which we are dealing with sensitised persons.

It is difficult at present to give a satisfactory explanation of the striking effect of vaccines in pneumonia. We know that in this disease, antibodies are produced late and cannot be found in the first two or three days. It may be that the dead bacteria are more easily utilized as antigen than the living organisms owing to the latter producing aggressins which interfere with antibody production. The action differs from that produced by intravenous injection of a foreign protein in that there is no rise of temperature and no rigor. At the same time the action of a vaccine does not seem to be so highly specific as that of a serum, for in my earlier cases a vaccine made from a single strain of pneumococcus produced results not appreciably different from a polyvalent vaccine containing typed organisms. Vaccines made from primary cultures are more powerful than those made from subcultures, and it seems to be of more importance to have an active vaccine rather than one less active

but containing all the types of pneumococci. I have found no advantage from using detoxicated vaccines. There is no object in using a dose of 1,000 millions of a detoxicated vaccine when a dose of 100 millions will produce the same or a better result. Rosenow has used autolysed pneumococci in doses of 20 billions, but in twenty-four patients injected on the first day only five had a crisis on the following day, and the average duration of fever was 3·5 days. There is much evidence to show that a vaccine in which the organisms have been as little altered as possible in process of sterilisation has great advantages over others.

Serum Treatment

Many attempts have been made to make a satisfactory antipneumococcus serum. Cole and his fellow-workers at the Rockefeller Institute have succeeded in obtaining an effective serum against type 1 pneumococci, but it is highly specific and useless in infections caused by the other types of pneumococci against which, so far, no effective serum has been obtained. Unfortunately, these latter types are responsible for two-thirds of the cases of pneumonia and two-thirds of the deaths. Before serum can be used in the treatment of a patient, the type of infecting organism must be determined, and this requires access to a well-equipped laboratory and a delay of twelve to twenty-four hours. The serum must be given in large amounts up to 250 c.cm. or more, and it is injected intravenously. The injection of this large amount of foreign protein is frequently followed by general constitutional reactions. There may be a rise of temperature of 3°, rigors, difficulty in breathing, and cyanosis, quite apart from the danger of anaphylaxis in patients already sensitised to horse serum. To avoid this danger an intra-dermal skin test should be performed, and if positive the patient must be desensitised. A week or more later there may occur the group of symptoms called serum disease, comprising fever, skin rashes, œdema, pains in the joints, and glandular enlargement. Reports on the use of serum in type 1 pneumonias show a considerably reduced mortality. Cole in one hundred seven cases had a mortality of 7.5 per cent; Nichols in sixty-three cases a mortality of 8 per cent; Greenway, Bœttiger, and Colwell in one hundred twenty-five cases 5·6 per cent; and Tenny and Rivenburgh 14.7 per cent in sixty-eight cases. As with vaccine, the earlier the serum is injected the better the result, and it is of doubtful value in patients who are very ill in the later stages. Anti-pneumococcic serum is not antitoxic and is not comparable to anti-diphtheritic serum. It does not appear to have the same rapid effect as vaccine treatment given in the early stages. Apparently the amount of antibodies which can be supplied artificially is less than that formed by the stimulation of the antigen in a vaccine unless excessive doses of serum are injected. Although

serum treatment may become more practically useful in the future, in my opinion vaccine treatment gives more decided results and is free from the unpleasant and even alarming immediate and late effects often seen after the injection of serum.

Foreign Protein Therapy

Attempts have been made to abort pneumonia by the injection of foreign proteins such as milk, typhoid or gonococcic vaccines, phylacogens, peptone, etc., either intramuscularly or intravenously. Small series of cases have been reported, and they show that the immediate thermal reaction is often followed by general improvement and signs of beginning resolution. But the thermal reaction was often severe and even violent, and it does not seem justifiable to use these methods when better results can be obtained without these disadvantages.

Symptomatic Treatment

In the early stage the relief of pain and sleeplessness is important. Leeches, when they can be obtained, give quick relief to pleuritic pain. Light and frequently changed linseed poultices are also useful, but must not be allowed to embarrass breathing. Considerable muscular energy can be expended by raising a poultice weighing two pounds or more on the front of the chest forty times a minute. Care must be taken that the poultices are not kept in place by a tight binder, as is often the case when applied by the unskillful. Antiphlogistine answers the same purpose, but it is not unusual to see badly scarred chests after its use. In a few cases with very severe pain I have separated the pleural surfaces by the introduction of a small quantity of oxygen. This is not difficult to those accustomed to artificial pneumothorax treatment, and I was favorably impressed with the immediate relief given. Counter-irritation in lobar pneumonia should not be continued after pain has been relieved, but in influenzal diseases with much congestion and bronchitis it can usefully be continued. Ten grains of Dover's powder in a saline draught will relieve both pain and sleeplessness. Paraldehyde is probably the safest hypnotic, and can be given in doses of 1 or 2 dr. in very sweet tea. But its highly nauseous taste does not add to the comfort of the patient and makes food distasteful. Opium has been regarded with disfavor, but its use in the early stages of lobar pneumonia and later when there is firm consolidation, so long as there is no interference with the air entry into the other portions of the lung, is quite safe. In influenzal cases more care is required. In those with definite areas of bronchopneumonia and absence of bronchitis or œdema it may be given for the first two or three nights, but in the diffuse cases with general bronchitis or bronchiolitis, œdema, or cyanosis it should be withheld. In the

severe cases with great excitement and struggling and in post-critical delirium hyoscin is the only drug which is likely to be effective. It should be given in doses of one-hundredth of a grain hypodermically. Although it has been much condemned, my experience with it has been fortunate. When it is ineffectual we may be compelled to give morphia as well, in which case it should be combined with atropine.

Bronchitis kettles are not often seen with pneumonia but are used by some practitioners with influenzal broncho-pneumonia. The effect of saturating the air with moisture cannot be good for a disease in which the sputum is usually abundant, frothy, and watery. In cases with much bronchial secretion atropine may give great relief. If 1/100 gr. does not give the desired effect, it may be increased up to 1/30 gr. and repeated four-hourly for a few doses. But in the grave cyanotic influenzal cases with much respiratory embarrassment, I have found the most helpful treatment to be ammonium carbonate 10 gr. in a teacupful of milk every hour for six doses, repeating the course if necessary after omitting the drug for a few hours. This should *not* be given in lobar pneumonia.

It will be found in text-books that much space is devoted to the treatment of heart failure, but you will not find that any two text-books agree as to the remedies to be used. The fact is that though much can be done by early specific treatment, strict insistence upon absolute rest from the first, fresh air, and avoidance of overfeeding to prevent heart failure, we can do very little to treat it when present. Heart failure does not stand alone; it is but part of a general intoxication, and the circulatory phenomena are as much due to the action of toxins upon the medullary centers as to the poisoning of the heart muscle. With such a condition, drugs such as digitalis must be useless, and it is very doubtful if strychnine, camphor, caffeine have any action whatever upon the heart. An exception may possibly be made with pituitrin, 1 c.c. injected deeply into muscles for vasomotor failure, but little can be expected from that in severe heart failure. Digitalis is used by many from the first in large doses with the object of retarding the pulse, but the heart does not fail because of its rapidity but because of its intoxication. Digitalis can only slow this rate by poisoning the heart and blocking too frequent auricular impulses.

The heart can be best helped by giving it food and oxygen. The best food for the heart is sugar, and this can be given from the first as cane sugar, milk sugar, or honey along with the other foods. Intravenous injections of 10 per cent glucose are perhaps the most valuable of all remedies when circulatory failure has commenced. Oxygen is not in general favor because it is so badly administered. One still sees it given, in large hospitals as well as in private practice, by the futile method of

holding a funnel some inches away from the patient's face. When administered through a Haldane's apparatus or through a rubber catheter passed into the nasopharynx it is of decided value in lobar pneumonia, where the majority of alveoli and bronchioles are patent. It is useless in the severe influenzal cases with œdematous lungs and blocked bronchioles, but can then be given subcutaneously.

Alcohol is the most used of all drugs in pneumonia and influenza, and has the sanction of some distinguished authorities. There is no scientific reason for its use, which is mainly based on tradition and the popular idea that it is a stimulant. Apart from its very fleeting stimulating effect, produced reflexly by the irritation of mucous membranes, we know that its chief actions are to depress the nervous system and to inhibit antibody formation, neither of which is desirable in diseases whose toxins are also nerve depressants. The clinical experience cited in its favor is met with equally distinguished evidence against it.

It must be acknowledged that the high mortality of pneumonia and broncho-pneumonia will never be reduced by attempts to treat poisoned organs incapable of response, but by early diagnosis and prompt measures to prevent intoxication by immediate specific treatment and common-sense nursing. Expectant treatment in the early stages is often followed by harmful drugging in the later. Although we have much to learn about the natural processes of defense against the organisms responsible for these diseases, we are not making full use of the knowledge already attained. We have now at our hands weapons by whose use the mortality of pneumonia and influenzal broncho-pneumonia could be reduced to one-quarter of its present height.—*The Lancet Office, 1, Bedford Street, Strand, W. C. 2.*

DR. H. H. KOONS (*The Military Surgeon*, April, 1920) after giving his experience with the use of mixed vaccines in pneumonia concludes as follows:

"1. That a prophylactic dose of vaccine will confer immunity for from six to eight weeks.

"2. That as a remedial agent, vaccine, if given at the onset, will materially shorten and lessen the severity of the attack and pneumonia will be a rare occurrence.

"3. That vaccine given to a pneumonia patient will ameliorate the severity of the symptoms, hasten crisis, and cut the number of serious sequelæ to a minimum.

"4. That glucose, intravenously, combats acidosis, gives nourishment to the heart muscle, adds fluid to the body, and has a decided diuretic action."

JEAN MINET, Vaccinotherapy of Acute Pulmonary Affections, *Bull. et mém. Sod. méd. d. hóp. de Paris*, 38: 1557, Nov. 30, 1922 (*International Survey of Medicine*, Jan., 1923):

"The author formerly used 'adapted' vaccines in pulmonary congestion and broncho-pneumonia. After estimating the relative proportions of the various infecting organisms contained in the sputum a corresponding mixture of stock emulsions was prepared,

containing about 500,000 germs per cubic centimeter, which represented the 'adapted' vaccine. Since then, in order to gain time, Minet has made use of a stock vaccine containing 100 million pneumococci, 50 million streptococci and 350 million staphylococci per cubic centimeter, for the treatment of pneumonia, pulmonary congestion and broncho-pneumonia, and the results have been as satisfactory as with the preceding type of vaccine. It appears advisable to use a mixed vaccine even in ordinary pneumonia owing to the frequent association of the above bacteria. The effects produced by this vaccine varied but were always favorable. Sometimes there was a violent reaction with expectoration of the type seen in acute edema of the lungs and high fever, followed by a rapid cure, while in other cases the lesions seemed to dry up suddenly. There was sometimes no apparent immediate action but the general condition of the patient seemed nevertheless to be benefited, a remarkable state of euphoria being produced in very severe pulmonary conditions. It is suggested that sometimes the vaccine may cause a rapid immunization of the organism and in others a favorable crisis through shock action.

"In simple acute pulmonary affections with no cardiac, renal or other complications, the author always injects 1 c.c. of his stock vaccine in the supraspinous fossa and repeats this every day or every other day, until a cure is obtained. When the heart or kindeys are already affected by the infection, it is well to begin with 0.5 c.c. only, this dose being rapidly increased to 1 c.c. if the vaccine is well tolerated. In children it is advisable to begin with doses of 0.33 or 0.5 c.c."

DR. ARTHUR DARE, 2025 Walnut Street, Philadelphia, in a communication, April 27, 1923, says:

"Dear Dr. Sherman:

"I am enclosing a stenographic copy of an address delivered at the Medical Officers' Training Camp, Fort Oglethorpe, Ga., July 17, 1918, reporting 423 cases of pneumonia and broncho-pneumonia, treated with vaccine. Some of the important facts have been omitted, I find. The crisis in most of the cases of lobar pneumonia occurred on the fifth day of the disease.

"All of these cases reported I personally examined and followed from admission to their discharge; I have the records made at the time, and have only embraced those that I can vouch for.

"I have also a record of a number of cases of 'flu' treated at Camp Dodge, Des Moines, Ia., during the epidemic of 1918. Our organization, Evacuation Hospital No. 25, headed for France, was quarantined during this period, and I was placed on the pneumonia board and in charge of pneumonias with the medical chief of the base hospital.

"This material has not been tabulated but it can be done when the time presents if it is necessary. The results were excellent.

"I hope this material will be sufficient.

Yours very truly,

ARTHUR DARE."

STENOGRAPHIC copy of the notes taken at an address delivered at the Medical Officers' Training Camp, Fort Oglethorpe, Ga., July 17, 1918, by Lieut. Colonel Arthur Dare, Medical Corps U. S. Army, Chief of Medical Service, U. S. General Hospital No. 14, Fort Oglethorpe, Ga.:

"One of the big problems of the Medical Service has been the ACUTE RESPIRATORY DISEASES:

"ACUTE PNEUMOCOCCUS INFECTION, OR LOBAR PNEUMONIA, runs its course in five days—when there are no complications.

"The pneumonia that is secondary to measles, scarlet fever, meningitis, and occurring after surgical operations: BRONCHO-PNEUMONIA.

"The cases admitted as ACUTE BRONCHITIS; fever; type undetermined and influenza.

"From a special investigation of lobar pneumonia, we found the type of pneumonia in the largest number of cases was Type IV, a very severe infection with consolidation of many lobes; the next most frequent was Type II; next Type I, and last Type III.

"The broncho-pneumonia study gave pneumococcus, streptococcus hæmolyticus, staphylococcus albus, aureus and citreus, micrococcus catarrhalis and influenza bacillus.

"In the investigation of the influenza epidemic, occurring at Camp Forest, Fort Oglethorpe, Ga., completed and reported April 23, 1918, laboratory research found the bacillus influenza in 80 per cent of infections. From throat culture; from sputum stains and culture, they ran nearly parallel—80 per cent.

"Now to briefly outline our treatment of these cases, our laboratory, under the charge of Major Bergey, made up of a stock vaccine containing the bacteria most commonly present at that time, the object being to start an immunity as early as possible. An autogenous vaccine could not be made early enough to head off the complications. A PNEUMOCOCCUS COMBINED VACCINE containing pneumococci, 400 millions; streptococcus hæmolyticus, 200 millions; staphylococcus, mixed albus, aureus and citreus, 400 millions; micrococcus catarrhalis and B. influenza.

"Every case upon admission, presenting physical signs of respiratory infection, was vaccinated with 125 millions of this stock vaccine. A period of three days was allowed to establish an immunity, then 250 millions were given, and three days later 350 millions. A fourth dose was rarely necessary.

"Our pneumonia cases were treated in the open air, on the porches of the medical pavillions; they were guarded from cross infection by sheets between the beds, light masks were used in some cases where cough was pronounced, but strange as it may seem, cough was very much less noticeable than we had expected.

"Our theory was, that if we could head off the pus, we could eliminate many of the complications and sequelæ.

"It was either coincidence, or good treatment by the Ward Surgeons and nurses, or the action of the vaccine that our mortality in cases of Lobar Pneumonia, Type I, II, III, IV, and a total disability period of 21 days—318 cases with 20 deaths, or 6.3%—105 cases Broncho-Pneumonia with 9 deaths, or 8.5%. A total mortality in all pneumonias—423 cases with 29 deaths—6.3% mortality.

Cases of Pneumonia Associated with Pneumococci in Combination with Streptococcus Hemolyticus

TYPE	NO	DEATHS	MORTALITY
I	43	3	7.0%
II	54	4	7.4%
III	16	2	12.5%
IV	116	6	5.1%
No Reaction	89	5	5.6%
Broncho-Pneumonia	105	9	8.5%
TOTAL	423	29	6.3%

"All cases of Broncho-Pneumonia were treated with vaccine, and with such success that all patients with measles were given vaccine as a prophylactic upon admission, and either from coincidence or vaccine, we limited our development of Broncho-Pneumonia to such a noticeable extent, that it is routine treatment in this hospital to vaccinate upon admission.

"It has been a source of interest in returning cases to duty with foreign troops, to observe the number of sound men who have had Pneumonia and Broncho-Pneumonias. The Influenza cases were vaccinated upon admission and the tonsils and throat treated with nitrate of silver solution, 40 grains to the ounce and the period of disability was four days on the average.

"In treatment of these cases, the names of the patients were telephoned to the laboratory upon diagnosis and treatment carried out by the laboratory promptly, and according to roster.

"I was given permission by our Commanding Officer, Colonel Haverkampf, to limit the mortality in measles pneumonia which was climbing steadily. We have had his co-operation at all times. The Medical Department of the Army has permitted us to employ vaccine in Type II, III and IV pneumonias (for Type I pneumonia, Type I Serum was used), and we have had the co-operation of the laboratory, then under Major Bergey, and of the Ward Surgeons and the personnel of the hospital—the only possible way that success could have been obtained."

(About 20,000 doses of Sherman's vaccine formula 38 was supplied to Camp Dodge, Des Moines, Iowa, at the time of the influenza epidemic referred to in Dr. Dare's letter.)

MAJOR J. PRATT JOHNSON, M. C., D. A. D. M. S., S. A. M. C., Director Clinical Research Laboratory, Johannesburg, South Africa (*American Medicine*, March, 1919) goes into great detail concerning the advantages of polyvalent mixed vaccines in the prevention and treatment of respiratory infections and sums up his conclusions as follows:

"1. Anaphylactic and anti-anaphylactic phenomena play a very important part and are valuable guides in vaccine therapy, especially in diseases of the respiratory tract. Serologic tests are not satisfactory guides or reliable indicators of established immunity, or of practical service in the carrying out of treatment with vaccines or sera.

"2. The very important part played by symbiosis in bacterial infections of the respiratory organs cannot be too strongly emphasized. The clinical results of therapeutic and prophylactic inoculation with mixed vaccines lend strong support to these views.

"3. A constitutional weakness in the elaborate defensive organization against invasion by the causative micro-organisms of respiratory diseases indicates a pneumo-catarrhal diathesis. This constant diminished resistance can be successfully reversed by specific immunization with a highly multivalent mixed vaccine prepared from numerous recently isolated virulent strains of those pathogenic bacteria commonly conveyed in the air breathed. Non-specific treatment is of no avail.

"4. Roughly, less than 25% of cases diagnosed as pneumonia in general practice are due primarily to infection with pneumococcus, the proportion varying from time to time. In all cases of pneumonia, however, the condition is sooner or later a mixed infection in which any of the causative bacteria of respiratory diseases may be present. M. catarrhalis and streptococcus are the commonest in South Africa. Pneumococcus, B. Friedlander, B. influenzæ, streptococcus mucosus capsulatus, staphylococcus, B. septus are also regarded as important organisms in the etiology of pneumonia.

"5. Whatever theoretical objections may be raised to this statement, the clinical results in practice, both of therapeutic and prophylactic inoculation for pneumonia, with a mixed vaccine, afford overwhelming evidence as to the soundness of these views. The mixed vaccine used is prepared from 150 virulent isolated strains of M. Catarrhalis, streptococcus, pneumococcus, streptococcus mucosus capsulatus, B. Friedlander, B. influenzæ, B. septus and staphylococcus. Each organism is represented in a curative therapeutic dose, the actual dose used being somewhat less than the amount required when each organism is used separately.

"6. These views have been strongly confirmed and widely tested on a very large scale in South Africa during the prevailing epidemic of Spanish influenza, the very heavy mortality being due almost entirely to pneumonia. The mortality from pneumonia has been greatly reduced by therapeutic inoculation with mixed vaccines. Similarly prophylactic inoculation with larger doses of this mixed vaccine has reduced the incidence of influenza and prevented pneumonia, fatalities in individuals inoculated twice being rare.

"7. The failure of preventive inoculation against pneumonia with various pneumococcus vaccines is due to a false or incomplete conception of the etiology of the disease broadly diagnosed as pneumonia. This want of success is not due to faulty dosage of pneumococcus vaccine, or the absence of unidentified strains of pneumococcus. If pneumococcus vaccine was of definite value proof would have been forthcoming long since in view of the numerous experiments which have been carried out on a large scale.

"8. This failure is due to the fact that the etiologic significance of other microorganisms has not been recognized. The organisms in addition to pneumococcus are M. catarrhalis, streptococcus, streptococcus mucosus capsulatus, B. Friedlander, staphylococcus, B. influenzæ and B. Septus. That the incomplete and inaccurate views in regard to the etiology of pneumonia have survived so long is due to the modern development of water-tight compartments in medicine. The clinician is not a bacteriologist. The bacteriologist is not a clinician.

"9. Prophylactic inoculation with mixed vaccine prepared from the organisms enumerated will enormously reduce the incidence of pneumonia and other respiratory diseases (excluding tuberculosis) and largely abolish the mortality from these diseases. The actual composition of the vaccine and proportion of each organism represented in the mixed vaccine used should be decided from a close and extensive study of the bacteriologic flora found in respiratory diseases."

ADVANTAGES OF MIXED POLYVALENT VACCINES IN PNEUMONIA

DR. LEWIS K. NEFF, Clinical Professor of Medicine, University and Bellevue Hospital Medical College, and Doctors A. G. Sala and K. M. Kera.

"During the last weeks of January, 1922, at the time of the prevalence of epidemic influenza in New York City, we commenced the treatment of a series of cases of pneumonia at Harlem Hospital by the use of mixed polyvalent vaccines as an adjunct to our regular treatment. We have looked over the cases so treated, and have tabulated some notes in the accompanying charts. Some words of explanation and comment are, it seems to us, in order.

"The plan of vaccine administration was as follows: One initial dose of 1 c.c. of Sherman's mixed vaccine No. 38, containing Influenza Bacillus 200,000,000, Streptococcus 100,000,000, Pneumococcus 100,000,000, Micrococcus Catarrhalis 200,000,000, Staphylococcus Aureus 200,000,000, and Staphylococcus Albus 200,000,000 was given subcutaneously, followed by a similar dose in 6 hours. Four more doses of 1 c.c. each were then administered, 12 hours apart. The subcutaneous injections were made in a different region of the body each time, following the premise that the fresh, unburdened cells of the new locality would be best apt to manufacture antibodies under the vaccine stimulus. Following this initial course, if the temperature was still up, vaccines were usually continued in 2 c.c. doses, 12 hours apart. In some few cases, this second course was not instituted, even with the temperature still up, to see if any untoward febrile reaction might follow the stopping of the vaccines. On the other hand, in a few other cases, with the temperature fairly well done, vaccine treatment was kept up, to see what febrile reaction, if any, might be elicited by such treatment.

"As soon as a case came to the ward, diagnosed as pneumonia by the admitting physician or ambulance surgeon, the chest was examined, and if the physical signs, together with the respirations and blood count confirmed the diagnosis, vaccine treatment was immediately begun in some cases, not instituted at all in other 'control' cases, or postponed in a few other cases, where it was desirable for purposes of investigation to see what the patient could do with his own unaided immunizing powers.

"A white and differential blood count was done in each case before the first dose of vaccine was ever given. Other blood counts were made later. We think enough counts were made in each case to give an insight into the patient's powers of cellular defense.

"A general survey of the kind of cases we had to work with, is desirable. Our pneumonias came in after they had been ill for a little time, usually three days, and most of them had received no medical attention previous to their entrance to the hospital. These cases were also treated during the prevalence of epidemic influenza. It is now generally regarded that epidemic influenza is due to an unknown organism, probably a filtrable virus, which lowers the resistance to the pneumococcus and other organisms usually responsible for pneumonia. So, when epidemic influenza prevails, it is often difficult to estimate how much of the temperature and other toxic symptoms of a patient are due to the unknown virus of influenza. Now, whether lobar pneumonia be a pulmonary affair or a mixed septicemia with pulmonary localization, the antibodies that bring about the patient's successful defense, must do their work at the seat of the disease. Antibodies produced away from the lungs must be carried thither by the circulation. The lack of medical attention at the onset of the disease and for some time thereafter is obviously another handicap to the success of whatever treatment is instituted in the hospital.

"Pneumonia being a self limited disease with a definite course, it ordinarily shows such fixed mortality 25-35%, that any new drug, vaccine or serum, before laying claim to a definite place in its treatment, must do any or all of these things, (1) hasten the crisis, (2) prevent the spread of the pneumonic process, (3) offset complications in the lung itself and the pleural cavity (4) offset complications elsewhere, e.g., pneumoccccus meningitis, otitis, peritonitis, etc. (5) increase the body's immune bodies and thereby reducing the mortality rate.

"We may now analyze the effect of the vaccine treatment on different features of our cases so treated.

"(a) Temperature. The gentleman who so kindly furnished the vaccine for trial in our wards, claimed that in the ideal case, there ought to be a considerable fall in the temperature chart after three 1 c.c. doses of vaccine. The ideal case is the one where the administration of vaccine is begun as soon as the disease begins. From this point of view, none of our cases were ideal. Nor were ideal results obtained. We have purposely charted the T. P. R. after the third dose of vaccine. There was a definite fall in some cases, but qualifying remarks are necessary.

"Case V. On sixth day of disease when vaccine treatment was started, temperature 102.6°, pulse 130, respiration 42. Here the fall in temperature to 98° and the crisis after three doses of vaccine came all on the seventh day of illness, a favorable crisis day in pneumonias.

"Case VIII. Case came in hospital with entire right lung involved. Started vaccine treatment on third day of disease with temperature 105°. Two first doses were given at 6 hour intervals and four more doses at 12 hour intervals up to morning of sixth day. Temperature down to 102.8°. Vaccine discontinued for two days, temperature ranging between 101.4° to 103°. On eighth day temperature went up to 103.8°. Three double doses of vaccine given at 12 hour intervals and by the tenth day temperature 98.2°. Vaccine discontinued. Temperature stayed down 4 days. Lower left lung then became involved and temperature suddenly went up to 104°. One double dose of vaccine given but patient soon died. Since the temperature came down after the first six doses of vaccine, again rose after discontinuing vaccine for two days, came down to normal after three

double doses and remained down for four days. The question arises: would the temperature have gone up again and the left lung become involved if the vaccine had been continued, say, at daily or twice daily intervals after a normal temperature was obtained?

"Case XIX. Where this course was pursued, indicates that by pursuing this method this case might have been saved.

"Case IX. This patient's temperature on fourth day of illness when admitted to hospital was 104° and dropped to 98° in 24 hours, was 99.2° after the third dose of vaccine, then went to 102°, on the sixth day subsequently temperature was never higher than 101.5° and gradually returned to normal on twelfth day. Vaccine was given at 12 hour intervals during fifth, sixth and seventh days; none given during eighth day, two double doses given ninth and tenth days and one double dose given on eleventh day.

"Case XI. Admitted to hospital on sixth day of illness, temperature 104°. Vaccine treatment started on seventh day; first two doses 6 hours apart and four more doses 12 hours apart. Crisis came between first and second dose. There was a subsequent rise to 103.6° on tenth day but no spreading of the pneumonic process, with an uneventful recovery.

"Case XIII. Was admitted on second day of illness, lower left lobe involved, temperature 103.2°, pulse 119, respiration 24. Started vaccine treatment 15 hours after admission; on third day of illness, two 1 c.c. doses, 6 hours apart and four 1 c.c. doses 12 hours apart and two doses 2 c.c. each. Temperature on day vaccine treatment was started up to 105.4°, then gradually dropped down to 101° on the fifth day, on the sixth day up to 104° with a crisis on seventh day and normal temperature. Vaccines discontinued on sixth day. On eighth day temperature 104.2° with reinvasion of left lung. Vaccine again started in 2 c.c. doses 12 hours apart, temperature on eleventh day went up to 105° for a short time, then by evening of twelfth day temperature 98.4°. Vaccines discontinued twelfth day. Reinvasion on thirteenth day with temperature 103.5°. Vaccines again given in 2 c.c. doses at 12 hour intervals, giving seven doses with a gradual decline in temperature to 100°. Patient died three days later. The fact that the temperature declined with a crisis and a reinvasion took place with a rise of temperature two different times after vaccine treatment was discontinued is significant. The question naturally arises whether these reinvasions would have taken place if vaccine treatment had not been discontinued. Furthermore, since the temperature went up to 105.4° at 8 a.m. on the third day of illness, before the first dose of vaccine was given, it is a question whether this patient would have survived more than a few days without the vaccine. As it was, under the vaccine treatment, the illness was prolonged with several prospects of recovery.

"Case XIV. Came in hospital with signs of 'grippe.' Developed consolidation of left lower lobe on second day in hospital, after temperature came down to 100°. Vaccine treatment started on third day in hospital with temperature, giving two doses 1 c.c. 6 hours apart and four doses 12 hours apart, followed by four 2 c.c. doses 12 hours apart. There was a drop after the third dose to 101.4°, then up to 104.2° on third day of pneumonia. Crisis on fifth day of pneumonia with uneventful recovery and no spreading of pneumonia process.

"Case XV. This was a truly ideal case. Had started with 'grippe' symptoms four days before admission to hospital. Definite signs of pneumonia in left lower lung detected about 24 hours after admission to hospital. Without definite signs, on the strength of the temperature and blood count 1 c.c. of vaccine was given two hours after admission. Second dose 6 hours later, followed by four doses at 12 hour intervals. Vaccine treatment was started with a 104° temperature. After the third dose, it dropped to 99.6°, went to 104° for a short time next day, then rapidly came to normal on fourth day in hospital and made an uneventful recovery.

"Case XIX. This case was admitted on fourth day of illness with a temperature of 103.8°. Vaccine treatment was started on admission, giving 1 c.c. and another dose 6 hours later and four more doses 12 hours apart, followed by six more doses of 2 c.c., 12

hours apart. Temperature came to 100° after third dose, then up to 101.8° on third day, followed by crisis. Further vaccine administration produced no febrile reactions. Recovery uneventful. No spreading from right lower lobe.

"Case XXIII. Took sick with 'grippe' symptoms 6 days before admission. Onset of pneumonia determinable. Vaccine given 5 hours after admission. Six doses of vaccine given in usual manner in 3 days. Temperature dropped from 103.8° to 98° after fourth dose followed by rise to 102° and 102.8° and drop to 99.2° about 10 hours after sixth dose. After that never over 100.2°. Never over 99.8° in last five days. No spreading from right lower.

"Case XXVIII. Admitted to hospital on fourth day of illness. Lobar pneumonia, left lower, temperature 104.4°. Has T. B. sinus in neck and T. B. glands in neck. No T. B. found in sputum after 15 examinations. Vaccine treatment started at once. Six 1 c.c. doses given in usual way. After third dose temperature ranged between 103° and 101°. Vaccine discontinued for two days then, four doses 2 c.c. with Sherman's Non-virulent T. B. Vaccine in it. Temperature between 101° and 99° during ninth and tenth day. Vaccine discontinued. Became normal eleventh day. Up to 102° on twelfth day and septic temperature after that.

"In no case has there been a rise of temperature or increased pulse rate that could be ascribed to the vaccine injections. This applies to the cases when the vaccine was given during high temperature as well as when given after the temperature had come down. All in all, the temperature and pulse curve in vaccine treated cases as compared with the ordinary pneumonia curve is lower. This is well illustrated by working out an average curve of the charts of the eighteen cases treated in the male ward and the eight cases treated in the female ward which recovered, starting the curve on the first day of vaccine treatment, which was an average of 4.5 days after illness started, and comparing it with the average curve of the four charted cases that recovered which received no vaccine as shown by composite charts 1 and 2. The average temperature of the twenty-six cases on the first day of vaccine treatment was 103.1°, by the end of the second day 101.8°, by the end of the third day 101.6°, on the fourth day 100.5°, on the fifth day 100.1° and then steadily declined to normal. The average pulse on the first day was 115, the second day 105, third day 105, fourth day 98, fifth day 98, sixth day 90, then down to normal within a few days. This steady decline in temperature and pulse rate beautifully illustrates the steadying influence of the vaccine on the temperature and heart action. The combined curve on the composite chart No. 3 of the four charted cases that recovered without vaccines, on the other hand, shows an increase of temperature and pulse rate during the first day and a constant high pulse rate compared to the temperature throughout the illness. This steadying influence of the vaccine on temperature and heart action is even shown on the average curves in the five charted cases that died as shown by the composite chart No. 4. Here the temperature and pulse curve show a constant tendency to run lower, until the vaccine injections are discontinued, when they go up. The average temperature and pulse curve of the three cases that died without receiving vaccines (chart IV) certainly shows a greater irregularity in temperature and heart control with a much earlier fatal termination.

"(b) In the twenty-two cases where the vaccine was administered, only four showed a spreading of the pneumonic process.

"Case VIII. Came in with whole right side involved, signs in left lower first twelve hours before death and four days after vaccine treatment had been discontinued.

"Case XII. Spread from left lower to whole right lung. Vaccines were discontinued on sixth day, crisis with normal temperature took place on seventh day. Reinvasion with high temperature on eighth day. Vaccine treatment again started with double doses on ninth day. A second crisis on twelfth day. High temperature again developed with spread from left lower to whole right lung and death occurred three days later.

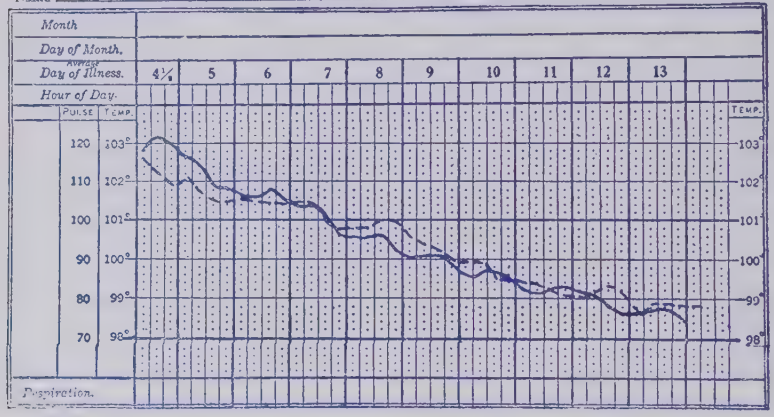
"Case XXI. Spread from right to left base.

"Case XXII. There was a reinvasion here on the eighth day after vaccine was stopped.

HARLEM HOSPITAL

History No._____

Name Composite Chart No. 1 Division Ward



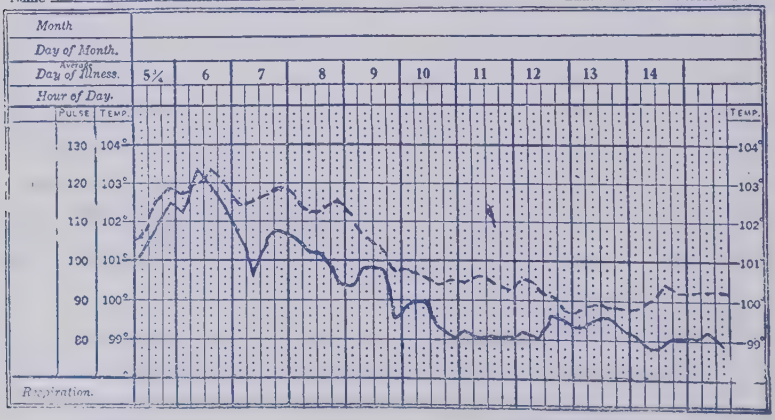
PULSE..... TEMPERATURE_____

Composite Chart of 26 Vaccine Treated Cases Cured
Average 4½ days ill before treatment started

HARLEM HOSPITAL

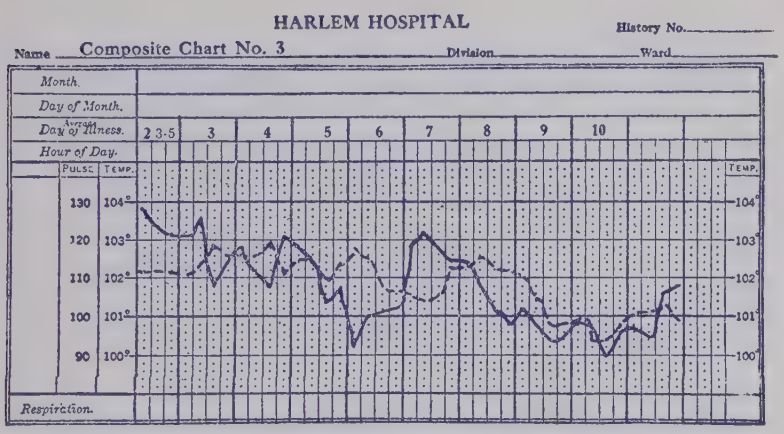
History No._____

Name Composite Chart No. 2 Division Ward



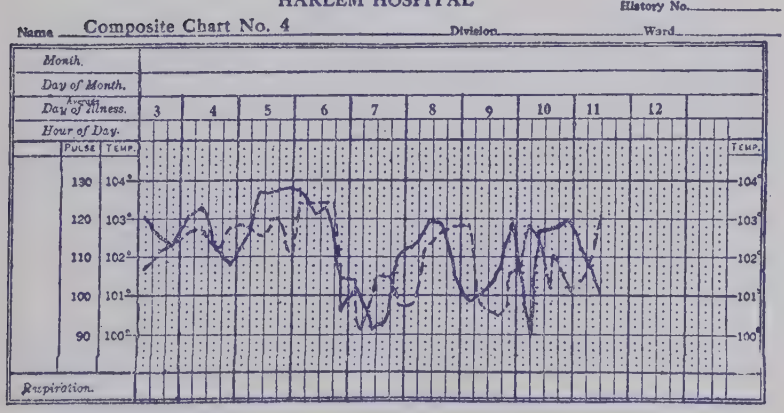
PULSE..... TEMPERATURE_____

Composite Chart of 4 Control Cases Cured
Average 5¾ days ill before treatment started



PULSE..... TEMPERATURE_____

Composite Chart of 5 Vaccine Cases, Died
Average 2 3-5 days ill before treatment started



PULSE..... TEMPERATURE_____

Composite Chart of 5 Control Cases, Died
Average 3 days ill before treatment started

"(c) There was no empyema in our vaccine cases. As a matter of fact, empyema in our ward this year has not been common.

"(d) The only case of otitis developed in a patient who had had several vaccine administrations. Case XXVII.

"(e) A glance at the different blood counts shows clearly that there was in all vaccine cases a definite rise of leucocytes in the blood, this leucocytosis persisting even after vaccines were stopped, and in some cases even when the temperature had been down for a few days. The average number of leucocytes in twenty-two cases on admission to the hospital was 21,663. After vaccine treatment for several days, this rose to an average of 25,095, an increase of 15 per cent. In four control cases, the leucocyte count on admission was 21,525. This is approximately the same as the vaccine treated cases on admission. After several days' stay in hospital, count dropped to an average of 17,250, a decrease of about 20 per cent. This would show an advantage of leucocyte activity of 35 per cent in favor of the vaccine treated cases.

"There was in no case any violent reaction from the vaccine. Even in cases where the vaccine injections were kept up after a decided fall in the fever chart, there was no rise in temperature with chill or any other expression of body reaction to foreign protein or toxin.

"The mortality in the vaccine treated cases was 16.3 per cent. In the cases treated without vaccines, the mortality was 42 per cent.

"Conclusions: In view of a more favorable mortality rate and absence of violent reactions and increase of leucocytes, the advantages of the routine use of mixed polyvalent vaccines in the treatment of pneumonia are apparent.

PREVENTION OF PNEUMONIA AND OTHER RESPIRATORY INFECTIONS

NEWSPAPER dispatches have recently stressed the effort made by the Medical Corps of the army to prevent pneumonia and other respiratory diseases by a system of voluntary vaccination, along the same lines adopted in the matter of typhoid vaccination, in 1909. The *Medico-Military Review*, November 1 and 15, 1921, a very interesting publication issued from the office of the Surgeon General, for the information of medical officers, contains a free discussion of the problem confronting the army and the efforts at present put forward for its solution. A letter from Col. J. F. Siler, of the Surgeon General's office, calls particular attention to the fact that no claims as to the value of this measure have been made, the intention being simply to work out some practical method of procedure which will minimize the occurrence of this disease in the army and at the same time which will contribute to the advancement of prophylactic medicine.

Those who have served in the Medical Corps of the army will recall the ever present dread of respiratory diseases, and the extreme steps taken for their prevention. Reliance has been primarily on general sanitary measures, such as the hygienic treatment of the nose, mouth and throat, of the recruit particularly; early isolation of cases; frequent inspection during epidemic periods; detection and isolation of carriers; adequate floor space in barracks; avoidance of crowding; proper ventilation; control of promiscuous expectoration; cleanliness, of the hands particularly,

and so on. With all of these precautions painfully carried out, the prevalence of respiratory diseases has been at times alarming. It has, therefore, appeared to those in authority essential that some more specific treatment be made available. It is not possible for soldiers to avoid contact with each other, as in civil life.

In the spring of 1920, observations were begun as to immunity conferred by attacks of influenza. The conclusion from incomplete data was that the disease itself did confer a degree of immunity, which, while temporary, was of some moment and served materially to reduce epidemics. Coincidentally efforts were made to produce immunity by the use of appropriate mixed vaccines, which seemed to afford some protection. In the fall of 1920, the administration of a pneumococcus vaccine was begun as a voluntary measure. While untoward conditions, as related to opportunity for scientific investigation, prevented the accurate conclusions desired, very interesting results were recorded. For one thing, and fortunately, the prevalence of pneumonia was greatly restricted over previous years. At Fort Meyer, Virginia, every other organization was vaccinated. There were five cases of pneumonia at that post during the season, all in the unvaccinated group. At Camp Meade, with a total strength of 2,319, 445 were vaccinated. Only one case of pneumonia occurred there, that being in the unvaccinated group and following measles, and the admission rate for other respiratory diseases was 94.38 per 1,000 in the vaccinated group and 97.65 per 1,000 in the unvaccinated controls. At Camp Travis, Texas, no pneumonia occurred in 1,366 vaccinated soldiers, while in a group of 14,296 not vaccinated there were nineteen cases. In other words, there was one case for every 752 not vaccinated and no cases in 1,366 vaccinated. As pointed out, these results are not conclusive, but they are interesting. We may further observe, that these efforts and observations may differ considerably from those offered as extenuation of the use by the profession of certain stock vaccines, urged by the manufacturers as a complete armamentarium in the treatment of respiratory diseases.

The vaccine used by the army now contains, according to Circular Letter No. 118, office of the Surgeon General, 6,000 millions of bacteria to the cubic centimeter, the total comprising 1,000 millions each of Types I and II of the pneumococcus, 1,000 million each of the two most common pathogenic types of the hemolytic streptococcus (Dochez and Avery) and 2,000 millions of the influenza bacillus (Rivers spinal fluid). Type III pneumococcus has been omitted because of its rarity. The influenza bacillus has been added because it acts as a pathogen for the respiratory tract, regardless of whether or not it is the cause of influenza.

Elaborate plans are being laid by Surgeon General Ireland for securing accurate data and reliable control, and it is to be hoped that results will

be comparable to those obtained in the matter of typhoid prophylaxis. Research workers in civil life are not favored with the opportunities for investigation available to the army surgeon, and their work will be definitely aided by the data secured from this source.—*Editorial Comment Texas State Journal of Medicine*, December, 1921.

SIR A. E. WRIGHT (*The Lancet*, March 29, 1919), among other things under the subheading "Results of Vaccine Therapy," says:

"The most dramatic and convincing—convincing because here no other therapeutic measures are employed as adjuncts—are the successes obtained in streptococcal lymphangitis, in streptococcal cellulitis—I am thinking of those cases which have already been incised without striking benefit—and in conjunctival phlyctenules."

Under Non-Specific Immunity he says:

"Let us just glance at the prospects which are here opened up. In the foreground stands the question of non-specific immunization. That immunization is always strictly specific counts as an article of faith; and it passes as axiomatic that microbic infections can be warded off only by working with homologous vaccines; and that we must in every case before employing a vaccine therapeutically, make sure that the patient is harboring the corresponding microbes. I confess to having shared the conviction that immunization is always strictly specific. Twenty years ago, when it was alleged, before the Indian Plague Commission, that antiplague inoculation had cured eczema, gonorrhœa, and other miscellaneous infections, I thought the matter undeserving of examination. I took the same view when it was reported in connection with anti-typhoid inoculation that it rendered the patients much less susceptible to malaria. Again, seven years ago, when applying pneumococcus inoculations as a preventive against pneumonia in the Transvaal mines, I nourished exactly the same prejudices. But here the statistical results which were obtained in the Premier Mine demonstrated that the pneumococcus inoculations had, in addition to bringing down the mortality from pneumonia by 85 per cent, reduced also the mortality from 'other diseases' by 50 per cent. From that on we had to take up into our categories the fact that inoculation produces in addition to 'direct' also 'collateral' immunization. This once recognized, presumptive evidence of collateral immunization began gradually to filter into our minds. Among, I suppose, many thousands of patients treated by vaccine therapy in private and in hospital, it happened every now and then that a patient was treated with a vaccine which did not correspond with his infection, and that the patient indubitably benefited. Again, it was not an uncommon experience for the subjects of a very chronic infection (such as pyorrhœa) who were treated first by a stock vaccine, and afterwards with an auto-vaccine, to assert that they derived more benefit from, and to ask to be put back upon treatment by, the stock vaccine."

DR. FREDERICK P. GAY, Professor of Pathology, University of California Medical School, Berkeley, Calif., in a special article prepared under the auspices of the Council on Pharmacy and Chemistry, says:

"It was natural from the beginning of the present pandemic of influenza that, with the apparent assurance that Pfeiffer's bacillus was the veritable cause of the disease, attempts should be made to produce an active protective immunity against this microorganism. With a growing conviction that no very extraordinary results were being attained, and with the discovery of other bacteria both in the complicated and in the uncomplicated cases, it was likewise reasonable that a mixed vaccine containing the most representative bacteria should be tried. We may now discuss the data that have accrued from these attempts, and try to evaluate them.

"A great deal of writing has been done on this subject, but much, perhaps the greater part of it, is of little or no value as evidence from which to draw conclusions. This doubtful mass of literature ranges all the way from opinions through clinical impressions to well arranged statistical material drawn from careful observation. The latter data themselves are again of unequal value; some of them represent results checked by only one or more of the essential controls, whereas others, a very few, fulfil the criteria of rigid experimentation. The discussion may be clarified by outlining what I myself should regard as complete data from which conclusions as to the value of preventive vaccination should be drawn; they are those recommended by the Special Committee of the American Public Health Association. These recommendations prescribe that the groups of vaccinated and unvaccinated individuals should be essentially the same in number; that the relative susceptibilities of the two groups as regards age and sex, exposure to infection and attacks of the disease should be the same; that the degree of exposure after vaccination should be of the same duration and intensity for each group, and finally that the groups should be exposed concurrently during the same period of the epidemic curve. It is realized that very seldom will the data offered fulfil all these prerequisites.

"Two main types of vaccine have been employed in the prevention of influenza: first of all, a vaccine composed of influenza bacilli most of them comprising numerous strains, and secondly, a mixed vaccine containing the organisms most frequently found in fatal cases of influenza, that is to say, in addition to the influenza bacillus, pneumococci, streptococci, staphylococci, and at times certain other organisms. We must consider our results first in relation to the types of vaccine employed, and again in respect to the effect of these vaccines, on the one hand in preventing influenza, and on the other hand in preventing its complications.

"The vaccine composed of influenza bacilli alone has been found by a few observers apparently to exert beneficial effects in preventing the incidence of the disease, notably by Duval and Harris and by Wallace. Other observers with perhaps even more carefully controlled experiments, such as McCoy, Murray and Teeter, and Wadsworth, attribute not the slightest preventive action to this vaccine.

"When we come to consider the use of mixed vaccines, we find at once more valuable and more enthusiastic reports as regards their preventive value. A whole series of observers—Rosenow, Cadham, Eyre and Low, Kraus and Kantor, Cary, and Minaker and Irvine—have apparently demonstrated a distinctly diminished incidence of influenza in the vaccinated as compared with the unvaccinated, and the particular writers to whom I have referred have for the most part carefully controlled their cases by a group of unvaccinated individuals. But it is not so certain in every instance that they have fulfilled the other requirements already outlined. McCoy, on the other hand, finds no beneficial effects from the use of a mixed vaccine in prevention.

"Mixed vaccines have been used, not only preceding exposure to influenza, but also during the course of the disease in the hope of preventing its complications. There is a steadily growing body of information, some of it of apparently considerable critical value, that would seem to indicate that a mixed vaccine containing streptococcus and pneumococcus in addition to influenza bacilli will notably decrease the pneumonia complications of influenza. Among the observers that may be mentioned are Kitano, Armitage, Dever, Boles and Case, Bezancon and Legroux, and Cadham.

"Cary, and Roberts and Cary, have not only prevented the occurrence of pneumonia by the use of mixed vaccine, but have actually produced a rapid cure of pneumonia during its course, particularly when the vaccine is administered intravenously. The striking results that they claim for this treatment they properly attribute to a non-specific protein reaction, such as has been obtained by other observers in typhoid fever and acute rheumatism. The non-specific nature of the result is rendered more certain by similar beneficial effects produced by Cowie and Beaven, who used a typhoid protein in place of the mixed influenza vaccine with equally good effect."

A TABULATED REPORT OF PREVENTIVE INOCULATIONS CONDUCTED BY DR. GEO. EDWARD FOLLANSBEE, CLEVELAND, OHIO, AT THE

AMERICAN STEEL AND WIRE COMPANY

October 22, 1918, Inclusive—Influenza Immunization Begun Oct. 21, Concluded Oct. 29

OBSERVATION ON 5797 EMPLOYEES

WORKS	No. Inoculations			1 Inoculation			2 Inoculations			3 Inoculations		
	No. of Men	No. Men Rptd. Sick	No. Days Lost	No. Men Inoc.	No. Men Rptd. Sick	No. Days Lost	No. Men Inoc.	No. Men Rptd. Sick	No. Days Lost	No. Men Inoc.	No. Men Rptd. Sick	No. Days Lost
Steel	436	42	581	411	45	517	485	30	331	513	7	71
Wire	390	40	702	235	18	272	345	15	234	420	6	110
Cuyahoga	492	10	227	595	20	291	507	6	85	296	1	16
Cent. Fces	78	6	87	179	20	282	209	10	237	206	2	31
TOTAL	1396	98	1597	1420	103	1362	1546	61	887	1435	16	228
Per Cent Men Sick		7.02			7.25			3.94			1.11	
Deaths		5			4			2			0	
Death Rate Per M.		3.58			2.81			1.29			0	

It will be observed that this work was done early during the influenza epidemic of 1918.

DR. W. O. SHERMAN, of Pittsburgh, Pa. (*Journal A. M. A.*, Dec. 21, 1918) gives one of the most valuable reports on the prophylactic immunization in epidemic influenza because it was carried out on a large scale in the 1918 epidemic from the beginning of its early development and in the Pittsburgh district, Sherman's Formula 38 being supplied and says:

"At the Homestead plant, there were 1,687 of the employees who were not inoculated; 588 of those, or 30 per cent, contracted the disease. The number of deaths was forty-two, a percentage of 2.5. There were 5,964 who received one inoculation; of these, 213, or 3.5 per cent, developed the disease. There were nine deaths among these, or a percentage of 0.15; 5,222 received two inoculations, and 714 developed the disease, or a percentage of 3.2 with four deaths. The death rate was 0.08. There were 4,720 that received three inoculations; sixty-six of these, or a percentage of 1.4, contracted the disease. There were no deaths in those with three inoculations. There were 4,007 who received four inoculations at the one plant, and these data are accurate; 108, or 2.8 per cent, contracted the disease, and there were two deaths, giving a death rate percentage of 0.05."

From this report it will be observed that the incidence of those contracting the disease and the mortality rate dropped very materially after the first inoculation. As compared with the uninoculated in the Homestead plant, there were proportionately twenty deaths per 1,000 employees, whereas among the inoculated receiving one inoculation there were only 1.5 deaths per 1,000 persons. Among those receiving two inoculations, there were 1.3 deaths per 1,000; those receiving three inoculations, no deaths and those receiving four inoculations one death per 2,000.

DR. JOHN H. SLEVIN, Detroit, Mich., (Ohio State Medical Journal, May, 1921) says:

"It is my experience that there is no method of treatment for erysipelas, which has proved to be clinically curative, until the advent of vaccine therapy.

Inefficiency of Local Treatment

"I have found no indications for internal medication in erysipelas, and Osler says there are none. In fact, all the text-books I have consulted damn with faint praise the internal treatment which each seems to find it necessary to suggest.

"Under local treatment, Osler says: 'Of local applications ichthyol is at present much used. The inflamed region may be covered with salicylates and starch. Perhaps as good an application as any is cold water which was highly recommended by Hippocrates.' The most recent publication that I have seen, which is Moorhead's 'Traumatic Surgery,' says: 'Local measures have been recommended almost without number and cures often ascribed to them with about as much basis as if they had been similarly used to hasten the desquamation of scarlet fever, measles or any other disease of self-limited type.' This agrees exactly with my opinion.

"Of local methods thought to act as cures I may mention the injection of antiseptics in front of the advancing margins.

"I early learned that the streptococci advance irregularly ahead of the typical margin and in the few cases in which I saw it used the effect was ludicrous, the disease appearing beyond the injected area on schedule time. Sloughs due to the injection have been reported. One method that appealed to me theoretically and to which I gave a thorough

trial was painting the involved area and a wide margin beyond with 85 per cent phenol later neutralized with alcohol. The successes were in no greater proportion than by palliative treatment and I stopped it after getting a superficial necrosis on the tip of the ear in one case and almost at the same time having a doctor, who had repainted his mother's leg because my application had not checked the advance report that she was voiding smoky urine containing casts and albumin. Once I saw a sort of lattice fence painted with 95 per cent phenol around the indurated margin. The erysipelas jumped the fence, roamed awhile and disappeared, leaving the fence to be erased by painstaking and pain-giving dressing. I have not used it myself. A somewhat similar method was painting a stripe or boundary board with iodine or silver nitrate about the inflamed area. To my eye it made a jarring color scheme and evidently increased the patient's subjective burning without affecting the course of the disease.

"It seems to me that the most objectionable treatment and apparently the one most frequently employed, outside of hospitals, is besmearing the patient's inflamed area with grease containing some mixture of ichthyol. This causes neither subjective nor objective relief, is a dirty malodorous mess that firmly adheres to the tender skin and makes a nasty scab during desquamation, especially where hairy surfaces are involved. Other ointments vary from the above chiefly in color. They are objectionable because difficult and painful to remove.

Value of Bacterial Vaccine Therapy

"In the last few months I have had a series of twelve cases of erysipelas under my care treated with bacterial vaccines which I wish to report. Six women, all past 40 years; six men, all past 30 years. The men had all been intemperate, indulging in alcoholics and therefore were most unfavorable cases. The women all gave a history of previous attacks, lasting from one to five weeks. In no cases were more than ten doses of vaccine given at daily intervals until cure was effected and in seven of the twelve cases cure was effected after the exhibition of the sixth daily dose of vaccine. In the cases where the patients had been afflicted previously, they all were charmed by the rapidity of recovery.

"The most recent case, that of a lady, initials W. H., age 65, had suffered two previous attacks, one of eight weeks and the other of six weeks duration. She was quite delirious when I was called. Eyes closed completely and face and head swollen out of all resemblance to herself. Temperature 104°; pulse, 140; respiration, 26. Made complete recovery after the tenth dose of vaccine and after the fourth dose patient remarked how wonderfully quick, as compared with former experiences, her return to the borderland of health was and she added that this attack in its very incipiency was the most severe and serious attack of all.

"In conclusion I wish to emphasize the therapeutic importance of bacterial vaccines in the treatment of erysipelas. There can be no question or clinical doubt of the value of a remedy that answers the provisions of two cardinal laws, in the practice of medicine, namely, 'Do no harm' and return your patient to health 'quick, entirely and pleasantly'."

DR. BURT R. SHURLY, Professor and Director of the Department of Rhinology, Laryngology and Otology, of The Detroit College of Medicine and Surgery, in a private communication dated May 26, 1923, says:

"My dear Doctor:

"Ever since the manufacture of mixed vaccines began and Dr. E. L. Shurly returned from a personal study with Wright of London, I have personally been greatly interested in endeavoring to determine the full value of vaccine therapy.

"After reading, and studying and making use of considerable experience, I am convinced the stock vaccines have a decided place and value. It is true that this must be scientifically censored from time to time and that rather than give a shot-gun preparation

in a wild sort of way for any condition that might be infectious, we endeavor to get a bacteriological status for our therapeutics. We have been working along these lines long enough to standardize and stabilize our method.

"I do believe that in some infections of the respiratory tract in well selected cases, vaccine therapy is of great value. It must be safe-guarded by the most careful diagnosis and of course principles of surgical drainage must ever come foremost.

"The results I have had are the reasons for my confidence in this selective therapeutic procedure."

Very truly yours,

BURT R. SHURLY.

DR. WM. SCHEPPEGRELL, President of the American Hay-Fever-Prevention Association, Ex-President, American Academy of Ophthalmology and Oto-Laryngology, Chief Hay-Fever and Asthma Clinic, Charity Hospital, New Orleans, La., in a communication, May 21, 1923, concerning the use of mixed vaccines, says:

"Dear Dr. Sherman:

"Replying to yours of the 17th instant.

"In my book on 'Hayfever and Asthma, Cause, Prevention and Treatment,' I make the following statement:

"If the patient applies for treatment during an attack of hayfever, the pollen extracts are usually ineffective, and a vaccine should be used.

"Our reason for using the vaccine during severe paroxysms is that at this time the patient is suffering, not only from the effects of the pollen protein, but also from the great increase in the pathogenic micro-organisms resulting from the lowered resistance of the respiratory membranes.

"The autogenous vaccines are preferable, provided they can be obtained of the proper standard and purity. When there is any doubt regarding this, the stock vaccines of unquestioned reliability should be given the preference.

"Further experience has caused no change in our views on this subject."

Very sincerely,

WM. SCHEPPEGRELL, M. D.

DR. J. FRANCIS WARD, Brooklyn, N. Y., Consulting Physician Craig Colony for Epileptics, formerly chief of Tuberculosis Service, Base Hospital, Camp Upton, N. Y., May 23, 1923, in a communication says:

"G. H. Sherman,
Detroit, Mich.

"Dear Doctor Sherman:

"In immunizing against hay fever, I always ascertain the pollen that is responsible for the protein sensitization and endeavor to complete my pollen prophylaxis a few weeks before anticipated onset of the disease and follow with your formula 36 completing my immunization about the time of the usual attack. This I term pollen vaccino-immunization.

"With prophylaxis I have had most gratifying results and uniform immunity. If I do not get a patient until after the onset of the disease, I use the indicated pollen and your formula 36 mixed vaccine and designate it pollen-vaccino therapy. In asthma, I endeavor to ascertain if the disease is due to pollen protein sensitization or is largely a microbial asthma. If I class the disease as strictly microbial asthma, I use your formula 36, but if I find pollen protein sensitization a factor, I use both the indicated pollen protein

and your formula 36 and I anticipate adding in the future formula 45 or 47 in cases of long standing, when I do not get desired results with the aforesaid treatment.

"The symptoms and pathology of whooping cough are the same as those of hay fever. In whooping cough, it is the upper respiratory tract, which is affected—the trachea and glottis. The majority of whooping cough cases occur in April, May, June, July, August, September and October, the season at which plant pollination is at its heighth.

"In prophylaxis and treatment, I endeavor to find the pollen protein present and add this to your formula 37 or 43. For prophylactic immunization, I advocate your formula 37 largely with the appropriate pollen protein (when found)—and in treatment, your mixed formula 43 with the indicated pollen protein, if found.

"Past experience emphasizes the urgent necessity for the control of whooping cough in the dangerous years of childhood."

Very truly yours,
J. FRANCIS WARD, M. D.

THE VACCINE TREATMENT OF ASTHMA[1]

IN a paper on the subject published in "The Journal of Immunology," July, 1923, Francis M. Rackemann and Lillian B. Graham summarize their work on the subject as follows:

Summary

1. The method of making autogenous vaccines and of treating patients with emphysema, chronic bronchitis and with bacterial asthma is described.

2. Ninety patients have been treated with autogenous vaccines. A predominating organism was found and used in 29 cases with good results in eleven and fair results in eleven. In sixty-one cases, there was no predominating organism but a selection from several autogenous vaccines was made on the basis of the local reactions following the test dose. Good results occurred in thirteen and fair results in fourteen.

3. Forty-one patients have been treated with stock vaccines, likewise selected on the basis of the local reactions, with good results in sixteen and fair results in twelve.

4. Whatever vaccine is used the fact that good results occur only in those cases where the various doses of the vaccine are followed by local reactions at the site of inoculation is definite and striking.

5. The importance of the local reaction plus the fact that the results with stock vaccines are as good or better than those with autogenous vaccines gives rise to the impression that the action of all vaccines in asthma is non-specific.

6. Of the entire series of one hundred thirty-one patients, 9 or 7 per cent have been "cured;" 31 or 22 per cent have been definitely benefited; 13 or 10 per cent have been helped somewhat; 24 or 18.5 per cent have been relieved temporarily but 54 or 41 per cent have not been relieved at all.

[1]From the Medical Services of the Massachusetts General Hospital.

7. Although good proof of a cure brought about by vaccines is lacking, vaccines do good in many cases. And at least until we know more of the fundamental pathological physiology of asthma, their use is reasonable and justifiable.

DR. J. LESLIE DAVIS (*Pennsylvania Medical Journal*, Feb., 1922) says that for some time he had only paid half-hearted attention to vaccine treatment of sinus and ear infections until a few days prior to his own illness he had read a very favorable report which impressed him sufficiently to give the vaccine treatment a trial in his own case.

In August, 1914, he developed an acute ethmoiditis of "a most virulent and fulminating type" on both sides. Within twelve hours, a profuse purulent discharge had developed which soon became pure pus. He made a microscopic examination of the discharge and found numerous streptococci and staphylococci. Without waiting for an autogenous vaccine, he procured a mixed stock vaccine, containing these organisms and started treatment at once. This was within thirty hours after the onset of symptoms. He says: "Within twenty-four hours after the injection of the vaccine, every symptom seemed conservatively fifty per cent better." The vaccine treatment was continued. By the fifth day of the disease he says: "The discharge had entirely ceased, the nasal congestion had subsided sufficiently to permit of free respiration and I felt practically well." His usual method of other treatment was meantime also employed.

The favorable results in his own case induced him to give the vaccine treatment with mixed stock vaccines further trials and as a result of seven years' experience says:

"I shall state at the outset that my own experience, during the past seven years, with vaccine therapy as an aid in the treatment of sinus and ear infections, particularly with stock vaccines in acute cases, has been most satisfactory and has established in me a confidence in their value which no amount of conflicting testimony could easily shake.

"During those seven years I have tried to keep reasonably familiar with the literature upon the subject, and in my practice to be ever watchful for the much heralded dangers; but with each passing year I have continued to gain increasing reassurance with regard both to the safety and to the uniformity of results derived from vaccines administered, not promiscuously, nor as a specific, but as a most important accessory measure in the treatment of all acute suppurative infections of the sinuses and of the middle ear and mastoid.

"Supposing, however, that if in my earlier reading I had run across only such articles as were written by some of the ultra-conservative, warning of the grave dangers connected with the administration of any vaccine, or of the absurdly unscientific procedure of treatment with mixed stock vaccines and of the utter folly of expecting beneficial results from the latter, I likely should have concluded that my own results were purely 'dumb luck' and that I had miraculously avoided wholesale manslaughter. On the other hand, had I missed those articles and found only the opposite extreme I might have wondered whether or not I was criminally neglectful in not having treated all my patients for everything with vaccines.

"That may be an exaggerated characterization of the extremists, whose influence, after all, may be very necessary factors in the evolutionary stages of any new principles toward an eventual consummation of rationality. That between the two extremes, however, there lies a middle course, which any careful physician may follow with safety to a definite, desirable end in the treatment of a frequent and ofttimes serious type of disease, I believe there is ample evidence to sustain. Furthermore, I believe that the best interests of the public will be served when the general practitioner, the family physician, urban and rural, as well as the specialist, discovers that stock vaccines can be used to a degree of safety equal to that of the majority of the most frequently employed official pharmaceutical preparations, concerning which there is no question of propriety, and that there are certain classes of acute infections which respond to vaccines more effectually than to any other known treatment and in proportion to its early administration, for, as a rule, the family doctor is the one who sees those conditions first."

In conclusion he says:

"Since it is undoubtedly true that the longer the delay in administering the vaccine, the greater the difficulty in effecting a cure of acute sinus and ear infections, I maintain that the commercial producers and distributors of vaccines of high quality are rendering the medical profession an admirable and, let us hope, also dignified and ethical service."

PROPHYLAXIS OF WHOOPING COUGH

MILLER urges immunization of children against whooping cough. In Akron, Ohio, use was made of bacterin of a strength of 5 billion Bordet bacilli to 1 c.c. in doses of 2½ billion followed by 4 billion three days later. In Miller's opinion the proper strength for either prophylaxis or treatment is at least 5 billion to the mil. Failures with Bordet bacillus in the treatment of cases are due entirely to insufficient dosage administered at too-long intervals. A safe principle in the use of whooping cough bacterin is, "the younger the child, the larger the dose required." However, no case has failed to respond if the injection was given not later than forty-eight hours after the preceding one and the dose doubled each time. Miller believes that public health authorities are justified in promoting immunization against whooping cough just as they are urging immunization against typhoid fever.—*Journal A. M. A.*, October 29, 1921.

VACCINE IN THE TREATMENT OF WHOOPING COUGH

PERHAPS one of the most justly dreaded and serious diseases of childhood is whooping cough, not even so much for its immediate effects, although it is a disease of high mortality, but more so for its complications and sequelæ, particularly tuberculosis, and debility. Until the discovery of the specific agent of this disease—the Bordet-Gengou bacillus—nothing could be done by way of prophylactic treatment, and the active treatment hadto be entirely empirical and was largely unsatisfactory. In any event, the disease is highly infectious, and isolation must be carried out rigidly, even against suspected cases, for it is they who are always the most potent factors in the spread of disease. For successful prophylaxis or satisfactory treatment of active cases early diagnosis is essential; and

until diagnosis is established, the sputum and the vomitus must be particularly guarded from contact with others. Infection with whooping cough is by the so-called droplet method, and if contacts can be kept free from the patient's discharges, there is no likelihood of infection. Because other catarrhal diseases often give paroxysmal coughs, a positive diagnosis can be made only from culture.

"The vaccine treatment should be instituted the moment the disease is suspected. When the paroxysms are fully developed, treatment is not satisfactory. Failure from the vaccine treatment for whooping cough when diagnosis is not made from cultures is often due to the fact that the paroxysmal cough is not due to the Bordet-Gengou bacillus. The influenza bacillus is particularly likely to cause it. On the other hand, there are many strains of the Bordet-Gengou bacillus, and a pure culture of one strain will be of no avail in treatment when infection is caused by another strain. The administration of pertussis vaccine is harmless, and there is no danger of producing by it any anaphylactic reactions, and so an increase of symptoms, rather than amelioration of them. While the treatment of the disease with the vaccine during the paroxysmal stage is not as satisfactory as in the earlier stages, yet the severity of the paroxysms is much lessened and the disease much shortened. The dosage used in active or in prophylactic treatment is practically identical. In active cases it may be continued for a week or ten days—injections every other day. Usually dosage is commenced with five hundred million. Then one, two and three billions every other day in succession. The administration of the vaccine to all who are exposed will be found to reduce contact infection in a very large degree. There is no reason why with isolation and prophylactic dosage to every possibly exposed child, the disease should not eventually be reduced to a negligible number.

"While ordinarily pure cultures are used in the preparation of the vaccines, some of the proprietory vaccines are polyvalent, composed of the Bordet-Gengou bacillus, the influenza bacillus, the streptococcus, the staphylococcus.

"Finally, in condemning failures with the use of the vaccine in the treatment of the active cases, it must not be forgotten that when the use of the vaccines is commenced late in the disease, the damage to the body or the inception of complications and sequelæ have already set in, which the vaccine treatment can neither remedy nor repair.—Editorial, Boston Medical and Surgical Journal, April 4, 1918.

DR. HERMAN M. APPEL and Otto J. Bloom, New York (*Archives of Pediatrics*, March, 1922) after considering the problem of caring for whooping cough cases in conclusion says:

"In a disease so dreadful as whooping cough and so fatal in its immediate, and so

disastrous in its late consequences, whose etiology and epidemiology are known, and yet whose mortality is constantly on the increase and against which all methods have proven of so little use, any new means of combating it is worthy of all serious consideration, especially when such means is logical and founded on etiologic grounds. . . . . In a low-grade toxemia, however, such as whooping cough, the injection of the vaccines will throw the balance in favor of the body as is clearly demonstrated by the fact that after the third and fourth injections, there is an aggravation of the clinical picture; which at the same time gives an impetus to the further production of anti-bodies and from then on, the body is able to take care of itself and improvement is noted. Such a means we have in whooping cough vaccine. In those cases where it has failed to give satisfaction, it is probable that the strain of organism used in the vaccine was different from that producing the disease, or that a mixed vaccine was not used since secondary invaders are always present with the pertussis bacillus, or that an inert vaccine was used or the dosage not sufficiently large. In the closing paragraph of the Weekly Bulletin of the New York City Health Department for November 6, 1920, the Department urges the prophylactic inoculation of children in institutions and states that it may mean the saving of many lives and that the reaction to the vaccine is negligible; while health authorities of other cities advocate the use of mixed vaccine both for prophylaxis and especially for treatment. The average duration of the disease, as given by authorities, is from 45 to 100 days—with vaccines, the duration has been cut down to about 30 days, the severity has been mitigated, complications prevented and mortality reduced. Should its prophylaxis and cures be far from 100 per cent, any remedy that accomplishes all the above is a better remedy than any that has hitherto been put forward and should be used. Pertussis vaccine has done all this and has, therefore, established itself as a definite scientific entity of almost, if not actual, specific value in the treatment of whooping cough."

DR. HARRY S. BERMAN, Director of Whooping Cough Clinic, Detroit Dept. of Health (City Health Bulletin, Detroit Department of Health, May, 1921) in part says:

"If any apparently healthy child is brought in soon after exposure to a case of pertussis, two doses of vaccine are given as a prophylactic measure, one week elapsing between injections. The vaccine employed is that of the Bordet-Gengou baccillus and the dosage is approximately two and four billions for the respective doses. If evidences of a cold are manifested in the patient, a vaccine combined with the common pyogenic bacteria is employed, and injections are repeated at intervals of three days or more. . . . . .

"It is unfortunate that some physicians refuse to encourage the use of whooping cough vaccines, while others discourage the parents when it is requested, thus forcing them to seek assistance at the various clinics.

"It is the method of these clinics to refer the case back to the family physician, but the mother sometimes states that her doctor will not administer the vaccines, and she has come to the clinic for that reason.

"Many physicians hesitate to give vaccines to children owing to the possible anaphylaxis. This danger has been overestimated. No unfortunate results have been observed.

"Children tolerate vaccines exceptionally well. The younger the child the less the fear for any reaction. Newborn babies tolerate the maximum doses of vaccines equal to that of an older child without apparent bad effect. Physicians are prone to give too small a dose to produce results, fearing that a large dose may cause an unfavorable reaction.

"I can, therefore, safely recommend the administration of pertussis vaccines to children of any age. Physicians should insist upon giving the vaccine treatment in known infections and urge its use as a preventive among exposed susceptible children."

PROFESSOR JOHN O. POLAK (Journal A. M. A., Nov. 22, 1911, p. 1739) in part says:

"Autogenous vaccines of a single strain have given me unreliable reactions. This, I think, can be explained by the fact that the coccus is attenuated in its strength and, after it has produced its first reaction, the leucocytes become more or less accustomed to the particular variety of coccus, and are less liable to effect a defense than when a vaccine of polyvalent strain is introduced.

"Mixed vaccines of reliable laboratories have given better results than when a single variety was used. This has been shown repeatedly in the blood-picture when an autogenous vaccine of single strain used in large doses, even up to 500,000,000, has failed to increase the leucocyte count or diminish the polynuclear percentage, the mixed vaccines of several strains have promptly produced a marked leucocytosis. Even colon bacillus infections, such as the infection of a pelvic hematocele by the colon bacillus, have yielded more promptly to mixed vaccines of polyvalent strains than when a single autogenous germ has been used.

"One characteristic which has been noted throughout all of our experience is that, even before any definite effect has been noted on the temperature, the well-being of the patient seemed to be improved by vaccine injection."

PROFESSOR J. DANYSZ, Chief of Service, of the Pasteur Institute, Paris, in his book on "*The Evolution of Disease*" shows the value of mixed stock vaccines prepared from organisms isolated from the large intestinal content in the treatment of a large variety of diseases. The fact that he isolates the organisms from the intestinal content does not signify anything. A colon bacillus isolated from the feces would certainly not be a better organism to prepare a vaccine from than a colon bacillus which is isolated from an appendicular abscess or a colon bacillus peritonitis. Pneumococci, streptococci and staphylococci which are responsible for infections of the upper respiratory tract are constantly being swallowed with saliva and food. There is no evidence that their passage through the digestive tract will improve them in their properties for immuno production when made into a vaccine. This so-called entero-antigen prepared by Professor Danysz is for all practical immunological purposes identical with Sherman's combined colon bacillus, streptococcus pneumococcus staphylococcus vaccine (Formula 35).

In describing results obtained under the sub-heading of General Reactions, page 175, Danysz says:

"The first striking phenomenon after the first, or the first few injections or ingestions of an autogenous or heterogenous preparation, is the rapid change in the patient's general condition. A direct action on the nervous system is nearly always observed which is shown by lassitude, a need for sleep, relaxation and rest, a general lull which is in no wise disagreeable, which may last several hours, rarely two or three days, and is usually followed by a long period (several weeks or months) of surprising exhilaration. The patient feels himself 'being born again,' he feels a surprising need for physical and mental activity, and can undertake without fatigue, work, which a few days before would have seemed beyond his strength. Sometimes, the period of lassitude is so short and slight that the period of exhilaration seems to appear all at once. In other, less frequent cases, the first doses of the preparations are followed by headaches which may last for several hours, by chills, or by a slight rise in temperature. Still more rarely, the symptoms of

the disease are seen to increase slightly. Asthmatics may have a more violent attack, the itching dermatosis are aggravated, psoriasis plaques become darker; but these aggravations never last long, are not contra-indications for further treatment, and are always followed by appreciable and rapid improvement. At the most, it may sometimes be necessary to diminish the dose. If this is necessary, only 1/10 or even 1/100 is given."

All these beneficial effects from a combined colon bacillus vaccine have been recognized for a long time and were designated as the tonic influences of vaccines. I. M. Mullick (*Calcutta Medical Journal*, Aug. 1911. page 41) gives a detailed report of the increased metabolic activity in a variety of cases, as indicated by increased elimination of waste products as found in the urine during the twenty-four hours. In part, he says:

"These facts certainly give us some light as regards the changes within. Very probably it is this: (1) That vaccines stimulate metabolic activity, increase elimination of waste and build tissues; (2) That they hasten catabolism, especially of weak and unhealthy tissues and help the building of healthy ones. Even in old people, this is evidenced; but in the young, with their tissues in a higher state of vitality, this vital response is the most marked."

DR. V. DABNEY (*New York Medical Journal*, Feb. 10, 1912, page 275) offers a plausible explanation of the tonic effects of vaccines, by means of Ehrlich's side chain theory and, in part, says:

"Naturally when the toxins are numerous, numerous receptors are pre-empted by them, and the metabolism of the body suffers proportionate detriment. Thus, by destroying these toxins, the vaccine renders available for food assimilation receptors heretofore occupied with toxin assimilation. The apparent effect of vaccine therapy on metabolism seems to bear out this theory."

In an editorial in *The Bacterial Therapist*, (Jan. 1915), the writer said:

"The general tonic effects of a vaccine may readily be demonstrated by giving a few doses of a combined vaccine, Streptococcus, 100,000,000; Pneumococcus, 100,000,000; Staphylococcus Aureus, 300,000,000; Staphylococcus Albus, 300,000,000; Colon Bacillus 200,000,000, in a case where general tonics are usually prescribed. It will be found that a feeling of well-being soon develops, associated with a keen desire to take food and a good digestion and assimilation to take care of it. With a demand for an increased food supply well taken care of, tissue cells have a better opportunity to develop and eliminate diseased conditions. In the treatment of chronic localized infections, with vaccines, we are often in doubt whether the beneficial effect obtained is due direct to its immunizing influence or to a general tonic effect. In many cases, no material improvement in the infected area will be observed until the general health has materially picked up, as shown by an increase in body weight and other evidences of general improvement, after which the lesion begins to clear up."

Professor Danysz has employed this mixed vaccine prepared from organisms isolated from the contents of the large intestine in the treatment of many diseases including dyspepsias, constipation, enteritis, chronic appendicitis, sigmoiditis, urticaria, eczema, psoriasis, scleroderma, asthma, emphysema, rheumatism, dysmenorrhea, leucorrhea, mild chronic albuminuria, disturbances of the menopause, neurasthenia, melancholia, insomnia, migraine, general fatigue and cases of localized tuberculosis, of skin and other parts of the body. All these conditions have been cured or markedly improved by the administration of this vaccine.

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